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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 39.] 1942. [No. 6.

SUMMARY OF RECENT ABSTRACTS.*

V. LEISHMANIASIS.

VISCERAL.

Epidemiology.

STEPHENSON (p. 250) reports on an epidemic of kala azar in the Sudan which began in 1932 and lasted for about eight years. In three years, at least 300 cases occurred in a population of 8,000, and the fatality rate was 80 per cent. Few recovered even among those admitted to hospital and given the standard treatment. It is thought that the epidemic arose from contact between the Dinkas of the area concerned and the Maabans, in whom an outbreak was reported in 1923.

HOEPPLI (p. 252) notes that although sporadic cases of kala azar have been reported from West, Central and South China, the real home of the disease is north of the Yangtse valley. Canine kala azar is common in Peiping, and if it can be established that the canine disease of North China is identical with human kala azar, the dog will have to be regarded as a reservoir of the human disease, as it is in the Mediterranean area. CHUNG (p. 252) takes up this point, and argues that recent study has brought increasing evidence of the identity of the human and canine disease in this area. This evidence is convincing :—In Peiping there is a very close association between cases in dogs and in man ; in a small village the identification and treatment of all human cases was not followed by disappearance of the disease, and it was later found that the dogs were infected and appeared to act as reservoir ; hamsters cured of one infection show some immunity to the other, and the same appeared to be true in one human case ; complement fixation tests cannot differentiate the two ; the parasites are morphologically identical and are equally pathogenic to experimental animals, producing identical reactions ; *Phlebotomus chinensis* is as readily infected by the one strain as by the other. CHÜNG and LI (p. 570) report further developments of the investigations

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1941, Vol. 38. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

in villages near Peiping. Close association between canine and human kala azar was found and there is strong presumptive evidence that the dog is the reservoir of human disease.

Galliard (p. 570), however, though not disputing the general conclusions arrived at by Chung, points out that in the legations' quarter of Peiping, although canine kala azar is common, the human disease is rare.

Clow (p. 569) states that kala azar is widespread in the Shensi province of Northern China.

Mitra (p. 251) reports that the situation in North Bihar, as regards kala azar, is acute, and that in this area 83,961 cases were treated in 1937.

Mazza (p. 251) refers to a few cases of kala azar which have been found in the Argentine.

Mello (p. 571) reports the finding of leishmania in smears from ulcers on a cat in Brazil, but could not determine whether they were *L. brasiliensis* or *L. chagasi*.

Aetiology.

Young (p. 253) reports that after a Chinese strain of *L. donovani* had been injected into a Chinese hamster, the animal acquired a generalized infection, and that at a later stage there developed a tumour of the foreleg, adherent to the periosteum. This consisted of macrophages and fibroblasts, with leishmania, and was of the same nature as the tumours which have been noted in infections of animals with *L. infantum*. It has been thought that tumour formation of this kind was characteristic of *L. infantum* infection, enabling it to be distinguished from Chinese strains ; the present finding throws doubt on the validity of this distinction.

Chu and Zia (p. 572) state that Chinese hamsters can easily be infected with *L. donovani* by intratesticular inoculation, and that the parasites can sometimes be found by intratesticular puncture as early as the fifth day. Hu and Ishii *et al.* (p. 254) report that with the Japanese striped squirrel *Eutamias asiaticus* the infection rate after inoculation of *L. donovani* is as much as 100 per cent.

Ishii (p. 254) reports on experiments in which *L. donovani* and *L. tropica* infections were induced in animals by administration or injection by different routes. Emulsions of infected liver were usually successful in inducing infection ; flagellates from culture were usually unsuccessful.

Adler (p. 255) has produced infection in two of six patients suffering from inoperable cancer, one with injection of cultural forms of the leishmania of kala azar, the other with emulsion of infected hamster spleen. He discusses the possible effect of human serum, which normally has a lytic effect on the parasites, in preventing infection attempted in this manner.

Ishii *et al.* (p. 258) show that *L. donovani* is capable of passing through the placenta, to cause infection in the young of infected mice.

Pai and Hu (p. 571) report that *L. donovani* will not multiply within the cells of chicken, hamster or human tissue cultures.

The question of the identity of *L. canis* and *L. donovani* in North China, and its epidemiological implications, are discussed above (*Epidemiology*).

Transmission.

SMITH, HALDER and AHMED (p. 256) have gone far to prove the transmission of kala azar by sandflies. In their first paper they describe a method for the maintenance of *Phlebotomus argentipes* on nutriment other than blood, demonstrating, incidentally, that blood feeds are not necessary for the satisfactory development of leishmania after first infection. In the second paper the authors show that the sandflies may become blocked, as fleas become blocked with plague bacilli. Blocked sandflies cannot ingest blood, and it is assumed that in their efforts to do so they discharge dislodged flagellates into the skin. Blocked flies are found only among those attempting to feed a second time on blood. In the third paper the authors describe transmission experiments. *P. argentipes* were fed upon a patient with kala azar, and were then maintained for 10 days on a diet of raisins. At the end of that time they were offered a blood meal on experimental animals. Of 5 hamsters and 8 mice used, all except 6 mice became infected. It was shown that complete blockage of the flies was not essential for transmission, but that one animal, bitten by blocked flies only, acquired a very heavy infection. There is no evidence that the virulence of the leishmania increased during development in the flies, but since it is known that human serum has a lytic action on leishmania, it may be that flies which take blood during the period of leishmanial development produce less intense infections than those maintained on fruit juices. These results, which are much better than those achieved in earlier experiments, are what would be expected of *P. argentipes*, since it was found to be so closely connected, epidemiologically, with the spread of kala azar.

HOEPPLI (p. 252) shows that the Chinese strain of *L. donovani* develops in *Phlebotomus chinensis*, which readily becomes infected when fed on infected hamsters and dogs, but less readily when fed on man, in whom there are fewer leishmania in the skin. CHUNG (p. 252) points out that in N. China *P. chinensis* is readily infected with *L. donovani* and that migration of flagellates forwards to the pharynx and proboscis is common. *P. sergenti* var. *mongolensis*, on the other hand, is not so easily infected, and the infection seems to persist only if blood is present in the stomach.

PARAENSE and CHAGAS (p. 572) state that, in South America, *P. longipalpis* and *P. intermedius*, when fed on dogs with kala azar, become infected with leptomonads. That these are actually derived from the dogs is indicated by the fact that generalized leishmaniasis has been induced in hamsters by the injection of ground-up, infected flies.

HOEPPLI (p. 252) considers that the fact that leishmania may be found in nasal secretions, urine or faeces does not throw any light on the epidemiology of kala azar. [It will be remembered that in the Sudan leishmania have been found in nasal secretions and certain animal experiments indicated that contact infection, without the intervention of any vector, was possible. See this *Bulletin*, 1937, Vol. 34, pp. 40, 567.]

Pathology.

GATTO (p. 259) gives reasons for the view that the anaemia of kala azar is due, not to an increase in the haemolytic process, but to defects in blood production which result from changes in the bone marrow.

HU (p. 256) recalls that in kala azar certain intercurrent infections, such as pneumonia and cancrum oris, may be followed by complete

disappearance of leishmania from the body. With this in mind, he gave repeated injections of bacteria, horse serum or beef broth to infected hamsters, but though there was some evidence of increased resistance, in no instance was the infection prevented. Two types of enlarged spleen were found : one very large, with scattered nodules of reticulo-endothelial cells containing few leishmania ; the other less enlarged, with fewer reticulo-endothelial cells, not collected into nodules, but laden with leishmania.

AJELLO (p. 570) points out that, in dogs, leishmanial ulcers are indistinguishable macroscopically from traumatic or trophic ulcers, that they are often the only sign of the disease observed, and that they usually occur on areas of skin exposed to trauma. In all the cases observed, visceral lesions were found and it is concluded that the parasites, with their predilection for reticulo-endothelial tissue, invade the skin and internal organs with equal readiness.

LIEU (p. 255) states that after intracerebral inoculation of infected spleen suspensions into hamsters, phagocytosis of the leishmania by the amoeboid microglia cells at the site of injection took place.

Diagnosis and Clinical Findings.

LAHA (p. 259) points out that the aldehyde test rarely becomes positive until the disease has existed for at least four months, and that certain other diseases may give results which cause confusion. He quotes a case in which the test was positive, but in which malaria alone was found.

GIRAUD and GAUBERT (p. 258), discussing diagnosis, point out that serological tests are not absolutely reliable, and that the presence of parasites should always be demonstrated. Spleen puncture gives the best results but is said to cause fatal haemorrhage in 1 per cent. of cases ; examination of sternal marrow, or tibial marrow in children, is safe and effective ; in children gland puncture is very good, but in adults is not always possible. BENHAMON (p. 258) agrees that sternal puncture is the method of choice, but points out that monocytosis of lymph gland juice is almost diagnostic even in the absence of leishmania. He also states that skin scrapings are often useful in diagnosis. In China CLOW (p. 569) advocates sternal puncture in preference to spleen or liver puncture. ANDREU *et al.* (p. 573) in Spain prefer sternal puncture to other diagnostic methods.

For diagnosis in dogs, HO *et al.* (p. 571) recommend and describe a method of ilium puncture.

DAVIES and WINGFIELD (p. 572) advocate gland puncture in diagnosis and describe the technique.

ISHII *et al.* (p. 258) show that inoculation of infected material into the anterior chamber of the eye of a rabbit produces heavy infection two to four weeks later. They suggest that this response may be employed for diagnostic purposes.

KIRK and MACDONALD (p. 261) record a case, in the Sudan, in which visceral, cutaneous and mucosal leishmaniasis were present ; lesions in the nose suggested espundia, cases of which have been reported before in the Sudan.

STEPHENSON (p. 250) notes that in the recent epidemic in the Sudan the disease was of acute type, with high mortality even when standard treatment with neostibosan and tartar emetic and, in some cases, anthiomaline, was given. Complications are common in the Sudan

type of kala azar, and KIRK and SATI (p. 260) mention intractable diarrhoea, haemorrhages, cancrum oris and lobar pneumonia. Concomitant infections are helminthiasis, malaria, amoebic and bacillary dysentery. CLOW (p. 569) notes that in China cancrum oris occurred in 14 of 100 patients either before or during treatment ; two-thirds of the patients with this complication died.

Treatment.

ADAMS and YORKE (p. 260) report apparent cure of an Indian within 6 weeks of treatment with 4 : 4′-diamidino stilbene. Splenic enlargement was quickly reduced and shortly before discharge from hospital no parasites could be found on examination of spleen or sternal smear material. NAPIER and SEN (p. 574), in Calcutta, give diamidino stilbene in doses to a maximum (for individual injections) of 0·001 gm. per pound of body weight. Relief for ill-effects is afforded by the use of adrenalin. The drug is an effective therapeutic agent in kala azar.

KIRK and SATI (p. 260) report on the treatment of 28 cases, in the Sudan, with diamidino stilbene. The total dosage necessary varies greatly, and the best scheme of treatment has still to be worked out, but the authors favour daily injections and used from 1·0 to 2·6 mgm. of the drug per kilo. of body weight. With this dosage toxic symptoms were negligible, but in the early stages exacerbations of the disease and skin lesions were not uncommon. The results were very good but some of the patients had not been long observed.

These authors (p. 573) give a later report on the same patients, in whom the results were highly satisfactory after a further period of observation, especially in view of the fact that most of them had one or more complications, including cancrum oris. In comparison with the results obtained in the Sudan with antimony, those achieved with 4 : 4′-diamidino stilbene and with 4 : 4′-diphenoxy pentane are undoubtedly good. Toxic symptoms were observed, especially with the latter, but were not enough to necessitate abandonment of the treatment.

KIRK and MACDONALD (p. 261) report success with 4 : 4′-diamidino diphenoxy pentane in the treatment of a patient in whom recurrence had taken place after a course of neostibosan. Ten doses of 80 mgm., and 13 doses of 100 mgm., in 10 cc. of water were given intravenously on alternate days, a total of 2·1 gm. There were no toxic reactions, and the patient was apparently cured.

KIRK and SATI (p. 261) report from the Sudan cases in which a finely punctate rash appeared, usually after a first or second course of treatment with antimony or diamidino stilbene. It appears only in those reacting favourably, and is therefore of some prognostic importance. A description of the rash is given, and it is stated that leishmania may be found in scrapings from the papules, but the eruption, unlike the post kala azar dermal leishmaniasis of India, tends to disappear spontaneously. It is thought that this phenomenon may be similar to the Herxheimer reaction in syphilis.

In the Sudan STEPHENSON (p. 250) found that patients with cancrum oris as a complication of kala azar stood a better chance of recovery if treated with ureastibamine than with neostibosan and tartar emetic.

DAVIES and WINGFIELD (p. 572) report a case of kala azar in which, after the administration of 2·6 gm. neostibosan, the complication of agranulocytosis occurred. Adrenalin produced an increase in the white

cells and was given frequently for some days. Complete recovery took place, and it appeared that the attack of agranulocytosis had had a curative effect on the kala azar.

WANG (p. 262) has traced the progress of leishmanial infection in the spleens of hamsters treated with neostibosan ; animals were killed at different stages of the treatment. Three stages were observed :— In the first there was proliferation of plasma cells and lymphocytes ; in the second degeneration of the host cells and disappearance of parasites ; in the third a process of repair. The important and characteristic changes were observed in the first three weeks. WANG and CHUNG (p. 575) report on the curative action of neostibosan on kala azar in hamsters, and note that after cure these animals show evidence of immunity against attempts to reinoculate the disease.

MITRA (p. 251) states that in Bihar, thorough treatment brings about cure in 95 per cent. of cases, and that the basis for a campaign of control is the establishment of intensive treatment in the affected areas.

CUTANEOUS (ORIENTAL SORE).

HALAWANI (p. 263) gives a list of endemic areas of oriental sore in Egypt. SALLAM (p. 575) refers to the fact that leishmanial skin affections are very common in the Minia province of Egypt, where the patients are mainly village farmers aged about 20. The ulcers are usually multiple on the face, arms and legs. He describes the clinical appearances and the course of the infection, and states that most of the sores respond to intravenous tartar emetic or to local application of 1 per cent. tartar emetic in vaseline.

MARCHIONINI (p. 263) has seen, at the hospital skin clinic in Ankara, a considerable number of cases of oriental sore from Central and Eastern Anatolia. He discusses the atypical appearances produced by secondary infection, and states that sores may resemble syphilis, tuberculosis, erysipelas or pyogenic skin infections.

AKAN (p. 263) notes that certain observers have successfully treated oriental sore with atebrin.

SENEKJI and BEATTIE (p. 576) have inoculated 227 persons in Baghdad with suspensions of cultural forms of *L. tropica* in an attempt to produce immunity. Of 200 of these a sore was produced in 198, and when complete healing had taken place, attempts at reinoculation were unsuccessful, though reinfection could be produced by injection of the parasites before healing of the primary ulcer was complete. Equally good results were obtained with both young and old cultures. TEMPLETON (p. 576) describes the course of an ulcer provoked by inoculation of cultural forms of *L. tropica.*

MUCO-CUTANEOUS (AMERICAN).

PESTANA, VILLELA, and their co-workers (p. 264) give an account of the epidemiology of muco-cutaneous and cutaneous leishmaniasis in the State of São Paulo, Brazil. Intimate contact with wooded country is not always necessary, but except for one town in which it is fairly common, the disease is rural in distribution, even in the zone of high endemicity. In the environs of the town mentioned, the species of Phlebotomus responsible for transmission are dense. ORSINI (p. 576) shows that muco-cutaneous leishmaniasis is a problem of increasing importance in Minas, Brazil, especially in the north-east. There are some purely cutaneous forms, but most are muco-cutaneous.

GEIMAN (p. 264) has studied the infectivity, for mice, dogs and monkeys, of *L. brasiliensis* from cutaneous lesions in Peru. In the chorio-allantoic fluid of the chick embryo *L. brasiliensis* showed much poorer infectivity than *L. tropica*.

MAZZA and CORNEJO (p. 577) report very good results from the treatment of American cutaneous leishmaniasis by means of infiltration of the sore with 5 cc. of a 10 per cent. solution of atebrin, combined with atebrin *per os*. Complete healing of one sore took place in 15 days, but the authors report failure in the treatment of mucosal lesions by this method. For them, combined fouadin and yatren medication remains the best. *Charles Wilcocks.*

FEVERS OF THE TYPHUS GROUP AND OTHER FEVERS.

LANCET. 1942. Jan. 31. p. 149.—**Rickettsial Infections in Man.**

The following table, reproduced from the current notes of the Army Pathology Laboratory Service, will be useful to readers of this Bulletin :—

Disease	Rickettsia	Geographical distribution	Insect Vectors	Possible vertebrate reservoirs.
Exanthematic typhus	*Rickettsia prowazeki*	Europe, Abyssinia, North Africa, Belgian Congo, Asia Minor, Persia, North China, Mexico	Louse *Pediculus humanus*	Man
Endemic or murine typhus	*R. prowazeki var. mooseri* (=*R. muricola*)	Worldwide	Rat flea *Xenopsylla cheopis*	Rat (squirrel, shrew)
Tsutsugamushi disease	*R. orientalis* (=*R. tsutsugamushi*)	Japan, Formosa, Malaya, Java, Sumatra, New Guinea	Larva of *Trombicula akamushi* (Japan), *T. deliensis* (Malaya), *T. deliensis* (India), *T. minor* (New Guinea)	Bandicoot
Trench fever	*R. quintana* (= *R. volhynica* and probably *R. weigli*)	North Africa	Louse *P. humanus*	Man
Rocky Mountain Spotted Fever (Eastern & Western forms)	*Dermacentroxenus rickettsi*	U.S.A.	*Dermacentor andersoni, D. variabilis*	Goats, hares, and other small rodents
Fièvre boutonneuse	*D. rickettsi* var. *conori*	Mediterranean zone	Dog tick *Rhipicephalus sanguineus*	Dog
South African tick typhus	*D. rickettsi* var. *pijperi*	South Africa*	Tick *Haemaphysalis leachi*	Dog ?
São Paulo rural typhus	*D. rickettsi* var. *brasiliensis*	Southern Brazil	Tick *Amblyomma cajennense*	Opossum
Q fever	*Rickettsia burneti* (= *R. diaporica*)	Australia, U.S.A.	Ticks *Haemaphysalis humerosa, Dermacentor andersoni, D. occidentalis, Amblyomma americanum, Rhipicephalus sanguineus* ?	Bandicoot

* Tick-borne typhus also occurs in Abyssinia and in Kenya where the dog tick *Rhipicephalus sanguineus* acts as vector.

CALDER (Royall M.). *Brucella, Pasteurella tularensis,* **and** *Proteus* **Agglutinins in Chronic Brucellosis.**—*Jl. Bacteriology.* 1941. May. Vol. 41. No. 5. pp. 593–604.

The existence of cross agglutination between tularaemia and brucellosis is now widely recognized, but there have been very few records of cross reactions between Brucella and Proteus organisms.

In a large series of patients, presumably suffering from chronic brucellosis, the author found positive Weil-Felix reactions (1–80 or over) in 13·5 per cent. of the cases.

The titre of *Proteus OX19* agglutinins was higher than the Brucella agglutinins in 65·9 per cent. of the cases.

The explanation suggested is that there is an antigenic relationship between Brucella and Proteus.

Mistakes in diagnosis are likely to occur unless attention is paid to the fact that ascending titres against Proteus are found in typhus but not in brucellosis. *John W. D. Megaw.*

NAUCK (E. G.) & WEYER (F.). Erfahrungen bei der Zucht von Kleiderläusen und der künstlichen Infektion von Läusen mit Fleckfieber. [**Methods of Louse Breeding and the Artificial Infection of Lice with the Virus of Typhus Fever.**]—*Zent. f. Bakt.* I. Abt. Orig. 1941. Aug. 28. Vol. 147. No. 6. pp. 353–364. With 4 figs. on 1 plate.

Detailed information is given of the technique of feeding lice at various stages of their development: gauze of varying degrees of fineness is interposed between the insects and their human host, the proper intervals between feeds and the duration of each feed are specified.

Among the other points stressed are the care that must be taken to breed the lice from stocks known to be free from other Rickettsiae such as *R. pediculi* and *R. quintana.* The human hosts must also be carefully selected to ensure their freedom from infection with *R. quintana.* The larvae are disinfected in 3 per cent. formol and their cages are sterilized once a week. The arm of the host is cleansed with alcohol before the lice are applied. The insects are kept in a moist atmosphere at a temperature of 32°C. The regular removal of dried faeces and dead lice is important. The faeces of the lice are examined at regular intervals to ensure the absence of contaminating Rickettsiae: the faecal particles are rubbed up with a little distilled water, smears are made and stained with Giemsa's reagent.

Full details are also given of the methods of infecting the lice and of examining them afterwards for the presence of Rickettsiae. Workers engaged on the investigation of Rickettsiae will find much useful information in this paper. *J. W. D. M.*

NAUCK (E. G.) & ZUMPT (F.). Versuche zur Uebertragung des epidemischen Fleckfiebers durch die Wanzen *Cimex lectularius* L. und *Triatoma rubrofasciata* De Geer. [**The Question of the Transmission of Epidemic Typhus by the Bugs,** *Cimex lectularius* **and** *Triatoma rubrofasciata.*]—*Zent. f. Bakt.* I. Abt. Orig. 1941. Aug. 28. Vol. 147. No. 6. pp. 376–381.

The authors have already concluded that *Cimex lectularius* is of no importance in the transmission of murine typhus [this *Bulletin,*

1941, Vol. 38, p. 443]. They now report that *Rickettsia prowazeki* injected into the coelomic cavity of bed bugs remained virulent up to 26 days though the organisms did not multiply. On the other hand emulsions of bed bugs which had fed on infected guineapigs did not infect other guineapigs when injected intraperitoneally. The disease was not transmitted to guineapigs by the bites of one and two bed bugs which had previously fed on infected guineapigs.

Similar tests were made with *Triatoma rubrofasciata* with negative or doubtful results. Both kinds of bugs were fed on infected patients but did not become infected; these results were not regarded as conclusive because the stage of infection of the patients was not considered favourable for the transmission of the virus.

Neither of the insects was thought to be suitable for the transmission of infection by *R. prowazeki* or for the preparation of a vaccine.

J. W. D. M.

Wetzel (Ulrich). Fleckfieber und Nierenschädigung. [**Kidney Lesions in Typhus Fever.**]—*Med. Klin.* 1940. Nov. 22. Vol. 36. No. 47. pp. 1312–1313.

A fatal case of typhus fever is described in which there was acute glomerulo-nephritis. The author states that the medical text-books do not lay sufficient emphasis on the damage to the kidneys in typhus fever; most of the writers suggest that this is an unimportant and infrequent feature of the disease.

Hertzog *et al.* (1935) are quoted as stating that in their experience of typhus fever epidemics in Chili, 67·5 per cent. of the fatal cases had acute glomerulo-nephritis, 22·5 per cent. had interstitial nephritis and only 10 per cent. had no kidney lesions. *J. W. D. M.*

Nauck (E. G.). Malaria und Fleckfieber. Vergleichende pathologisch-anatomische Betrachtung. [**Malaria and Typhus Fever. A Comparative Study of their Morbid Anatomy.**]—*Deut. Med. Woch.* 1941. Nov. 14. Vol. 67. No. 46. pp. 1259–1262.

The author points out that in both malaria and typhus fever the infection is introduced into the body by an insect and the chief lesions are localized in the vascular system.

The paper consists chiefly of a detailed comparison between the post-mortem changes found in the two diseases: the points of resemblance are emphasized but the differences described are so numerous that difficulty in diagnosis must be quite exceptional even when little information is available about the clinical features of the cases. The paper is of interest chiefly to pathologists. *J. W. D. M.*

Findlay (G. M.). **Laboratory Investigations on Typhus.**—*Proc. Roy. Soc. Med.* 1941. Dec. Vol. 35. No. 2. pp. 157–160. (Sect. of Epidem. & State Med. pp. 17–20). [31 refs.] [Summary appears also in *Bulletin of Hygiene.*]

This paper gives a clear and concise account of the laboratory methods employed in connexion with louse-borne typhus fever.

(1) *Diagnosis.*—Proof that a disease is typhus can only be obtained by the isolation and passage of the Rickettsiae through animals.

Two to five cc. of the patient's blood are allowed to clot in the refrigerator ; the clot is ground up in normal saline and injected intraperitoneally into a guineapig. In positive cases a febrile attack (40°C.) follows within 7 to 12 days. The virus is passed through a succession of guineapigs by intraperitoneal injections of 1·0 cc. of equal parts of 10 per cent. suspensions of the infected guineapig's spleen and brain. The animals show no naked eye changes but sections of the brain have small collections of round cells. In murine typhus the guineapigs get orchitis as well as fever and the virus can be transferred through rats which react very slightly or not at all to exanthematic typhus. In Mexico and China strains of Rickettsia have shown features intermediate between those of murine and exanthematic typhus.

The commonly used test for typhus is the agglutination of *Proteus OX19* : this should be positive within seven days though delays in the response have been recorded, even up to 19 days. Titres up to 1–5,000 are frequent, they may even be as high as 1–100,000. With *Proteus OXK* the reaction is negative or slight. In murine typhus the same reaction occurs, but usually to lower titres such as 1–200 to 1–2,000.

Positive Weil-Felix reactions also occur in undulant fever in titres of 1–80 to 1–240, but the progressive rise in titre does not occur [see CALDER above]. In typhus there may be a rising-titre agglutination against typhoid organisms ; in these anamnestic reactions the increase is almost entirely in the H agglutinins.

Agglutination of typhus Rickettsiae also occurs, but this test needs further investigation.

Typhus Rickettsiae injected intradermally into rabbits cause the formation of a nodule : if the Rickettsiae are mixed with serum from a recovered patient the nodules are not formed. The strength of the rickettsicidal bodies in a serum can be determined by using varying dilutions of the serum.

(2) *Specific Treatment.*—No effective chemotherapeutic treatment is known. Convalescent serum has not been very useful, but the serum of horses which have been hyperimmunized with Rickettsiae from infected mouse lungs is being tried ; there is a small stock of this serum in London. [See DURAND and BALOZET below.]

(3) *Prophylactic immunization.*—Live murine Rickettsiae attenuated by passage through the brains of mice and treatment with egg yolk, or by treatment with bile, and Rickettsiae from the faeces of infected fleas have been used on a large scale, but there are no accurate figures to show their value and they are not free from risk in view of the possibility that murine Rickettsiae may be converted into exanthematic Rickettsiae by passage through lice infected by biting a patient.

Weigl's vaccine, prepared from the phenolized intestinal contents of lice infected *per rectum* with *R. prowazeki*, appears to be of considerable value, but this method involves a delicate technique and also the employment of a large staff of immune persons on whom the lice are fed.

Killed Rickettsiae obtained from the lungs of mice infected intratracheally or from cultures made in the yolk sacs of developing chicks are under trial, but the results, so far, are described as " poor ".

Further research is needed to find a satisfactory method of immunizing against exanthematic typhus.

[Other workers, including FELIX, are by no means so pessimistic as Findlay about the prospects of success with killed rickettsial vaccines.]

J. W. D. M.

MUNK (Fritz). Zur Klinik des Fleckfiebers. [**Clinical Features of Epidemic Typhus Fever.**]—*Deut. Med. Woch.* 1941. Nov. 14. Vol. 67. No. 46. pp. 1256–1259. With 1 fig.

This paper deals chiefly with the signs and symptoms of the disease. Special stress is laid on the occurrence of very low blood pressure in severe cases; this is regarded as a factor of great importance in the production of gangrene of the skin which sometimes involves the whole of the foot.

The drugs recommended in treatment are, digitalis, especially in the early stages, caffeine, intravenous injections of glucose or glucose saline combined with adrenalin subcutaneously. Hot tea and dilute alcoholic drinks are considered to be useful: systematic warm-bath treatment is said to be of undoubted value. *J. W. D. M.*

DURAND (Paul) & BALOZET (Lucien). Sérothérapie antityphique. 120 cas de typhus traités par le sérum obtenu par inoculations de Rickettsias de poumon de souris. [**Serum Treatment of Epidemic Typhus Fever.**]—*Arch. Inst. Pasteur de Tunis.* 1941. June. Vol. 30. No. 1–2. pp. 1–22.

The authors have already described the preparation of anti-typhus serum by inoculating horses with Rickettsiae of murine and epidemic typhus obtained from the lungs of mice infected by the intratracheal route.

In experimental animals this serum was found to be much more effective than human convalescent serum.

The present note describes the use of the serum in 120 patients suffering from epidemic typhus fever: there were 140 comparable controls. The serum was tried only on patients for whom the date of onset could be determined accurately to be less than 10 days before the commencement of the treatment. A good deal of difficulty was often experienced in finding the date of onset, especially in patients whose mental condition was seriously affected. [This method of selection may have resulted in the inclusion of a larger proportion of mild cases in the group treated with serum than in the control group; it would be more difficult to elicit information about the date of onset from seriously ill patients than from those who had mild attacks.]

At first massive doses of 100 to 200 cc., often repeated on the second day, were given; later a single dose of 100 cc. was adopted as the routine procedure; occasionally a second dose was given a few days later.

In 140 controls admitted during the febrile period the fatality rate was 14·28 per cent.; in 112 indigenous patients treated with serum during the febrile period the rate was only 4·46 per cent. The average duration of the fever in a group of controls was 14·43 days. The duration in the treated cases ranged from about 10 days in 10 patients treated on the third and fourth days to about 13 days in 20 patients treated on the ninth and tenth days.

The treatment caused a decided amelioration of the symptoms and a shortening of convalescence. Certain complications were less frequent; for example, no case of parotitis against five in the controls, and one slight case of arteritis against four in the controls. On the other hand, pulmonary complications were just as numerous among the

serum-treated patients. Sulphonamides were not given because the authors had previous experience of disasters resulting from the use of sulphapyridine in the treatment of typhus fever.

Serum sickness, to the degree of causing a rise of temperature above 38°C., was seen in less than 10 per cent. ; it was of little consequence because it always appeared when the patients had already begun to gain strength.

There was little interference with the normal evolution of the Weil-Felix reaction, although in eight cases the maximum titre did not rise above 1–400 to 1–600.

The 8 European patients did not respond so well to the treatment as the indigenous patients ; one died of uraemia on the 11th day ; the duration of the fever in the others was 12 to 16 days except in one patient, aged 15, whose fever lasted only 9 days. *J. W. D. M.*

MACKENZIE (M. D.). **Some Practical Considerations in the Control of Louse-borne Typhus Fever in Great Britain in the Light of Experience in Russia, Poland, Rumania and China.**—*Proc. Roy. Soc. Med.* 1941. Dec. Vol. 35. No. 2. pp. 141–156. (Sect. of Epidem. & State Med. pp. 1–16). With 1 folding map & 4 charts. [Summary appears also in *Bulletin of Hygiene*.]

This paper, based on extensive personal experience, is of special importance at the present time.

The louse-borne form of typhus, so far as is known, is the only kind of typhus that is primarily a disease of man and that occurs as epidemics. The tick-borne, flea-borne and mite-borne types are endemic and localized, being accidental infections in man. Flea-borne typhus coexists with the louse-borne form in Mexico and Manchuria and there is evidence that the flea-borne virus, if transmitted through lice, can produce a disease indistinguishable from classical typhus, and so may originate epidemics of louse-borne typhus [see this *Bulletin*, 1940, Vol. 37, pp. 256, 267].

In Russia during the years 1919 to 1922 it was estimated that there were ten million cases of typhus with three million deaths. Great movements of population play a great part in spreading the disease ; non-immune persons are brought into infected areas or infected persons are brought into unaffected localities. Famine may be a more important predisposing factor than overcrowding. In endemic areas the curve of incidence starts in November or early December, reaching its maximum in March or April, and ends in June or July. In epidemic form the disease may occur at any time of the year : for example, in Spain in 1941 the epidemic started in April and reached its maximum in June and July. The disease is more fatal in non-endemic than in endemic localities ; it is mild in children and becomes progressively more severe till the age of fifty, after which it is " practically always fatal " in epidemics.

MURCHISON'S clinical description, written in 1873, cannot be improved on, but in epidemics the picture is often confused by the coexistence of other diseases such as relapsing fever, malaria, typhoid, measles, scarlatina, etc. Two helpful points in differential diagnosis are the rarity of the rash on the face and the fact that the rash does not come in crops. The distribution and time of appearance of the rash are very variable ; in mild cases and in children there may be no

rash. In sporadic cases diagnosis is seldom possible till the rash appears, usually about the fourth or fifth day. A rising-titre agglutination to *Proteus OX19* is the best method of diagnosis: a strong naked-eye agglutination in titres of 1–80 to 1–100 is regarded as diagnostic, but often it does not help during the first week. Retrospective diagnosis is sometimes important when the actual attack has not been seen: useful clues are persistent slowing of the mental process, transient delusions, localized paralyses, tremors of the hands, cardiac exhaustion and localized gangrene. Second attacks are rare and are mild when they do occur.

Administrative Control of Epidemics.

The personnel are notoriously exposed to grave risks, they must be young and must be provided with protective clothing, good arrangements for disinfestation and proper nourishment. Protective inoculation is seldom practicable in existing conditions.

An effective sanitary cordon must be established round healthy areas and every one who enters the protected zone must be disinfested. At one centre in Russia in 1921 refugees returning from Poland were delouse at the rate of 10,000 daily. The methods employed depend on local conditions, cyanide gas, hot air, steam, the Serbian barrel and hot ironing of clothes are mentioned. Provision of food for the affected population is often essential: in one area in Russia five million people were fed daily and extensive tractor cultivation was started so that the community was well nourished before the arrival of the next epidemic season.

For the control of typhus in Great Britain the following points are emphasized: every detail of the work of the preventive staff must be closely supervised by the medical officer in charge, the clothing recommended in Memo. 252 MED of the Ministry of Health should be worn, it must be changed after two or three hours of wear, masks and goggles are desirable to prevent the possibility of infection by the dried faeces of infected lice, rubber gloves and gum boots should be worn.

General delousing of the population at risk is even more important than the search for remote contacts, who are often impossible to detect because they may have been infected up to a fortnight or more before the diagnosis of the first case. Lice are transferred from man to man chiefly by actual contact; this may even be by rubbing shoulders in a crowded thoroughfare.

For the reception of patients a specially appointed hospital unit is needed: this should have a separate admission block with provision for delousing. The patient is first shaved, then bathed with a medicated soap, "possibly soft soap mixed with paraffine," which is thoroughly applied with a nail brush. A second disinfestation is carried out a week later to kill lice which may hatch out from nits.

For premises, cyanide gas is the best means of disinfestation; for clothes steam or hot air can be used.

The first case is often missed; in Glasgow from 1901 to 1926 there were 87 groups of cases, in 36 of these the first case was wrongly diagnosed. The M.O.H. must keep a constant watch for suspicious deaths and be in close touch with the doctors. Educational propaganda is of great value. [The paper is full of important information which cannot be adequately dealt with in a summary.] *J. W. D. M.*

Rose. Fleckfieberfragen bei der Umsiedlung der Volksdeutschen aus dem Ostraum 1939/1940. [**The Control of Typhus Fever in the German Colonization of Poland (1939–1940).**]—*Deut. Med. Woch.* 1941. Nov. 14. Vol. 67. No. 46. pp. 1262–1265.

This paper deals with the vast and complex problem of typhus prevention in a mass movement of 132,000 settlers from Germany to the newly occupied " ostraum " in Poland.

The settlers had to pass through regions devastated by war, swarming with impoverished refugees and notorious for the prevalence of typhus fever. Other adverse factors were the bitter cold of the season (Dec. 1939 and Jan. 1940), the lack of information about the prevalence of the disease in the localities traversed by the expedition and the recent occurrence of the disease in some of the areas from which the settlers had come.

An account is given in general terms of the elaborate measures of control which were adopted: the most striking of these was the establishment of a delousing station at the key point Littzmannstadt where all the colonists were deloused at the rate of 4,000 daily. Special observation posts were set up along the route and the migrants were kept constantly under close inspection by the sanitary authorities, the staff of which had been previously inoculated and thoroughly trained in their special duties.

Over-night camping in doubtful areas was avoided; as far as possible places inhabited by Germans were selected, but occasionally the parties halted in the open in spite of the extreme cold; temperatures as low as —45°C. were experienced.

Altogether there were nine cases of typhus fever: the patients were promptly isolated so that infection never spread to contacts.

No details are given of the preventive measures except that hot-air disinfestation is mentioned as being selected on general grounds and also because of its effectiveness in sterilizing the faeces of infected lice.

The author claims that the elaborate precautions were thoroughly justified by the results. *J. W. D. M.*

Steuer (W.). Ueber die Trockenblut-Probeagglutination bei Infektionskrankheiten und ihre Anwendung bei der Bekämpfung des epidemischen und endemischen Fleckfiebervorkommens. [**The Dry-Blood Agglutination Test in Infectious Diseases and its Application in the Control of Typhus Fever Occurring in Epidemic and Endemic Form.**]—*Muench. Med. Woch.* 1942. Jan. 9. Vol. 89. No. 2. pp. 33–37.

A method is described by which the most important agglutination tests can easily and quickly be carried out by the bedside and in the field.

No new principle is involved: tests were made on the same lines in the early days of the Widal reaction and are still in frequent use in the U.S.A. The technique as worked out by Dr. Kudicke and the author has already proved its value in the control of typhus fever in time of war. The method is as follows. The finger or ear-lobe is cleansed with alcohol, thoroughly dried and pricked with a Francke's or other needle: there must be a free flow of blood, squeezing is not permissible. The first drop is wiped off, then three droplets of blood

are taken up with a loop of platinum wire of 0·6 mm. gauge and a circular opening of 2·0 mm. diameter : the three droplets are spread in a row on a clean glass slide so that each forms a round smear of about one cm. in diameter. The droplets are very uniform in size, each containing about 0·003 cc. of blood, or about 0·0015 cc. of serum. The preparation when thoroughly dried at room temperature can be used for the test at any time up to several days : after long delay the agglutinins become weaker.

The bacterial suspensions used are (1) *Proteus X19*, killed at 75°C. : this keeps at room temperature for about two weeks ; if alcohol is added to make a strength of 20 per cent. it keeps for five months ; (2) typhoid and dysentery suspensions are killed by adding 0·1 per cent. formaldehyde, paratyphoid by adding 0·2 per cent. formaldehyde : these keep well for several months and do not involve rigid precautions to prevent contamination, so they can be kept in bottles and used repeatedly. Strokes made with a grease pencil between the smears prevent the suspensions from running together during the later procedure. To one of the smears 0·02 cc. of the suspension is added with a small measuring pipette, preferably of the Kahn type, to the next smear 0·04 cc. is added and to the third 0·08 cc. The suspensions are thoroughly mixed with the blood films, using the corner of a glass slide. The readings are made after 1, 5 and 10 minutes for typhus, after 1, 5 and 15 minutes for the enteric group, and after 10, 20 and 30 minutes for the dysentery group. Before and between the readings the slide is gently tilted up and down repeatedly. Evaporation can be prevented by placing the slide on a sheet of moist filter paper and covering it with the lid of a Petri dish.

When agglutination occurs there is a formation of fine to coarse granules or of greyish white floccules. Observations are made with a pocket lens or with low powers of the microscope.

Special tables have been prepared to show how the various results compare with those obtained by the standard tests, the dilutions employed, the time of appearance of the reaction and the size of the clumps being taken into account. [No description is given of these tables : in any case it would be desirable to carry out preliminary comparative tests, using both methods simultaneously.] The suspensions are kept at room temperature, in the dark ; if kept in the refrigerator agglutination is delayed.

For extensive surveys one drop of blood can be taken from each person, three droplets being placed on each slide. In one instance 200 specimens were taken in 90 minutes and the results determined in two hours. Cases positive to the addition of 0·02 cc. of suspension were fully examined later.

Many outbreaks of typhus fever were investigated by this method in Poland. Of 879 persons examined 206 gave positive reactions. Among the negative results were those of 10 persons who had just been attacked and of 23 who had been attacked within the previous year. Among the 206 positives 100 were in patients suffering from obvious attacks, 25 in convalescents and a number in persons who had attacks of fever simulating influenza. There were 35 patients who had no fever but in whom a more or less definite rash was seen ; there were six persons who also had a rash but gave negative reactions.

Most of the ambulatory cases were in children who usually were members of a family or community in which typical cases were occurring.

In persons who had never been exposed to the risk of typhus no reactions were ever observed which corresponded to Weil-Felix titres higher than 1–200, but in typhus areas there were rare cases in which higher titre reactions occurred in persons suffering from other fevers : these were probably of the anamnestic type.

The degree of importance of mild attacks in the transmission of infection is a matter which needs further investigation.

The dry-drop method has great possibilities and is worth serious consideration, not only for the detection of typhus fever but also for the discovery of carriers of enteric infection : in the latter case Vi bacillary emulsions are of special value. *J. W. D. M.*

Snyder (J. C.) & Anderson (C. R.). **The Susceptibility of the Eastern Cotton Rat, *Sigmodon hispidus hispidus*, to European Typhus.**—*Science.* 1942. Jan. 2. Vol. 95. No. 2453. p. 23.

The cotton rat *Sigmodon hispidus hispidus* is susceptible to the Rickettsiae of classical louse-borne typhus when these are introduced by the intraperitoneal, intracardiac or nasal routes ; young rats are more susceptible than old. Incubation of the Rickettsiae with serum from patients recovered from the disease prevented infection when the mixture was given by intracardiac injection in doses 5 to 50 times as great as the minimal lethal dose.

A still more susceptible animal is needed, but the cotton rat is more suitable than the guineapig for investigation of typhus. Its susceptibility to murine typhus is much less marked. *C. W.*

Macchiavello (Atilio), Cifuentes (Osvaldo) & Ovalle (Héctor). Influencia de la avitaminosis C en la evolución del tifo europeo experimental del cobayo. [**The Influence of Avitaminosis C on Experimental Epidemic Typhus in Guineapigs.**]—*Rev. Chilena de Hig. y Med. Preventiva.* 1940. Sept. Vol. 3. No. 2. pp. 111–120. With 1 chart. [18 refs.]

Twelve guineapigs were kept for 6 to 15 days on a diet completely devoid of vitamin C and were then inoculated by the intraperitoneal route with a strain of Rickettsiae of epidemic typhus.

Six of the animals survived for 7 days after inoculation ; in four of these the incubation period was 4 to 5 days instead of the usual 7 to 8 days.

The febrile attacks in five of the six animals ran the usual course : this was followed by a subnormal temperature and death. There was no scrotal reaction. Smears from the peritoneum and tunica vaginalis contained more Rickettsiae than were found in the case of control animals kept on a normal diet and inoculated in the same way, but the Rickettsiae were far fewer than in devitaminized animals inoculated with murine virus.

Although the results are in keeping with the view that vitamin C deficiency lowers the resistance to typhus infection they lend no support to the theory that deficiency of the vitamin in winter-season diets causes an increase in the number of inapparent attacks and a corresponding diminution in the apparent attacks. *J. W. D. M.*

Fraenkel (E. M.). **Typhus Fever.**—*Brit. Med. Jl.* 1942. Feb. 7. pp. 199–200.

This short paper contains remarks on various aspects of louse-borne typhus, chiefly with regard to epidemiology, transmission and protective measures. *C. W.*

Brazzaville [Afrique Française Libre]: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1940 [Ceccaldi (Jean), Director]. pp. 45–53.—Fièvres exanthématiques. [**Fevers of the Typhus Group in Brazzaville.**]

In 1936, murine virus was isolated from rats in Brazzaville (in Equatorial French Africa), and in the following year two cases diagnosed as murine typhus were reported. In 1938 a case of boutonneuse fever was recorded.

The present report deals chiefly with an outbreak which occurred among indigenous soldiers living in a rat-infested camp during the three months November 1939 to February 1940.

The agglutination responses of 20 patients are given: all were positive to *Proteus OX19* in dilutions ranging from 1–300 to 1–2,400. In some cases there were also feeble responses to *OXK*, *OX2* and *OXL*. Blood from three patients was inoculated by the intraperitoneal route into guineapigs; in two cases the results were completely negative, in the third there was fever and a pronounced orchitic reaction but no Rickettsiae could be detected in smears from the peritoneum or tunica vaginalis: subinoculations of the animal's brain into two other guineapigs gave inconclusive results.

Nine rats from the quarters of affected persons were examined with negative results.

On the strength of the orchitic reaction in one guineapig, the mild character of the disease and the serum reactions, the author regarded the outbreak as one of murine typhus. No mention is made of the presence or absence of lice in the patients or of evidence with a bearing on the possibility of man-to-man transmission.

Three attacks of a typhus-like fever occurred in Europeans during the same period; in all three the Weil-Felix reaction was completely negative. Guineapig inoculation gave a negative result in one case, in another there was a slight febrile reaction lasting three days with an incubation period of eight days. In two cases there was a rash.

J. W. D. M.

Heilig (Robert) & Naidu (V. R.). **Endemic Typhus in Mysore.**—*Indian Med. Gaz.* 1941. Dec. Vol. 76. No. 12. pp. 705–710. With 5 charts, & 3 figs. on 1 plate. [28 refs.]

Four sporadic cases of a fever of the typhus group are described; one of the patients lived in Mysore city, the other three became infected in separate villages within 15 miles of the city.

The temperature charts show that the attacks lasted from 15 to 21 days and that the fever at its height was for the most part remittent in type; it became intermittent about four or five days before its termination. A conspicuous rash was first seen from the eighth to the tenth day, it was macular and maculo-papular in all the cases and was widely distributed but was most abundant on the arms and

legs, including the palms and soles ; it was slight on the chest and face. Brown staining persisted at the sites of the spots for weeks or even months, especially on the hands and feet.

In three of the cases agglutination tests were done on two or three occasions between the 11th and 20th days against fresh Kasauli strains of *Proteus OX19*, *OXK* and *OX2* ; the responses were always negative. Wassermann, Kahn and Kline reactions were sometimes positive at the height of the rash but soon became negative.

Blood from one patient was inoculated intraperitoneally into guineapigs, which responded with a febrile reaction and swelling of the scrotum. Rickettsiae were found in smears from the tunica vaginalis.

Each of the patients had been living in a house infested with rats, some of which were trapped, but were not found to be infected. No lice were found and the patients denied having been bitten by ticks or mites. The authors state that " the diagnosis of endemic tropical typhus [presumably flea-borne] appears to be beyond doubt from the evidence given." Mite-borne typhus was excluded by the absence of any *tache noire* or lymphadenitis, and tick-borne typhus by the absence of evidence of tick bite as well as by differences in the clinical manifestations.

[The negative Weil-Felix reaction, the prolonged fever of an intermittent type and the character of the rash seem to the reviewer to be in keeping with a diagnosis of tick-borne rather than of flea-borne typhus ; the results observed in the guineapigs are equally compatible with either of these diagnoses. Mite-borne typhus cannot be excluded by the absence of local lesions though the negative responses to *Proteus OXK* make this diagnosis very unlikely. The complete absence of evidence pointing to the likelihood of tick bite is opposed to, though it does not completely exclude, the diagnosis of tick-borne typhus. Altogether these cases are good illustrations of the frequent difficulties encountered by practitioners in the differential diagnosis of the non-epidemic typhus fevers.] *J. W. D. M.*

Jocson (Catalino T.). **Typhus Fever : Some Unusual Clinical Manifestations.**—*Acta Med. Philippina.* 1941. Apr.–June. Vol. 2. No. 4. pp. 403–413. With 6 charts.

Within 3½ years 9 cases of " typhus fever " were seen among the students of the University of the Philippines. No two cases came from the same household and no contact was infected although the patients were treated in the general wards of the hospital without special precautions.

It was, therefore, assumed that the cases were of " tropical typhus fever " as described by Fletcher in 1925 [see this *Bulletin*, 1925, Vol. 22, p. 944].

Some of the special features of the attacks were—one patient had a rather slow onset ; one had purulent discharge from the left ear ; one had physical signs suggesting a pleural effusion ; some had symptoms strongly suggestive of an influenzal attack ; the temperature curve simulated that of typhoid fever ; there were no mental excitement, delirium or meningeal symptoms ; only three had skin eruptions, the spots were maculo-papular, chiefly on the trunk and neck ; there were no deaths, though some of the attacks were fairly severe.

[These were presumably cases of flea-borne typhus, usually known as murine or endemic typhus. The interest of the paper consists in its containing an account, illustrated by temperature charts, of this form of typhus about which there have been few clinical reports.]

J. W. D. M.

Boston (Roy J.). **Advances in Methods of Murine Typhus Control.**—*Amer. Jl. Public Health.* 1941. July. Vol. 31. No. 7. pp. 720–727. With 5 figs.

Murine typhus fever has recently become a major public health problem in Georgia, where the disease is widespread and increasing. Small towns and villages are specially affected.

The ideal method of rat control by complete rat-proofing of buildings is often impracticable, being slow and costly.

The method adopted was "vent stoppage" by which rats are prevented from getting into the buildings. The first step was to make a survey of all the premises in the affected localities, the information being recorded on special forms.

The materials chiefly used for stopping vents were galvanized metal sheets, galvanized wire cloth of ½ inch mesh, bricks and cement. The average cost for each business establishment was $3.

On completion of the work trapping of rats inside the premises was carried out at intervals. Garbage control was also effected.

As a temporary measure poisoning of rats by red squill baits was often carried out, but this was expensive and the results were only short-lived.

Many municipalities in Georgia have carried out vent-stoppage control; within a year the incidence of the disease was lessened in places where a rapid increase had been occurring before the adoption of the procedure.

J. W. D. M.

Reynes (V.) & Richard (J.). Manifestations nerveuses d'atteinte mésencéphalitique et syndrome de névrite ascendante au cours d'une fièvre typho-exanthématique. [**Nerve Manifestations due to Lesion of the Mesencephalon and Ascending Neuritis in an Attack of Typhus Fever.**]—*Rev. Méd. Française d'Extrême-Orient.* 1941. Mar.–Apr. Nos. 3–4. pp. 387–391.

In the report this interesting case is described as one of "an exanthematic typhus fever of the tropical typhus type": from the description it appears to have been one of mite-borne typhus fever of the tsutsugamushi type.

The interesting features of the case are as follows—(1) Very severe nerve manifestations appeared about the 11th day when the temperature was steadily falling. There was stupor and fibrillary twitching of the muscles for ten days, then the patient seemed to awake but had choreiform movements and intention tremor for seven days, after which he had a slight recurrence of fever for two days accompanied by lancinating pain in the right side of the neck, shooting down the right arm. There was also wasting and loss of power of the muscles of the right shoulder. During the following month there was steady improvement ending in complete recovery. The local nerve manifestations just described were apparently associated with the presence of a necrotic patch which was noticed when the patient was admitted on

the sixth day of his illness and was accompanied by localized lymphadenitis. This patch was a typical *tache noire* and was situated on the lower part of the neck on the right side.

(2) The agglutination response to *Proteus XK* first appeared on the 18th day and reached a titre of 1–1,600 by the 22nd day : the reaction became negative after six weeks. There was also a positive reaction to two strains of *Proteus X19*, this reached the titre of 1–1,600 about ten days later than was the case with *Proteus XK* : it also disappeared earlier. Higher titres than 1–1,600 were not tested, but presumably the reaction to *XK* was the stronger of the two. The reaction to *Proteus OX2* was negative throughout.

(3) The Kahn test became positive about the 22nd day and remained positive for about two months. There was no evidence of syphilis.

J. W. D. M.

Patiño-Camargo (Luis). Nuevas observaciones sobre un tercer foco di fiebre petequial (maculosa) en el hemisferio americano. [**New Observations on a Third Focus of Petechial (Spotted) Fever in the American Hemisphere.**]—*Bol. Oficina Sanitaria Panamericana.* 1941. Nov. Vol. 20. No. 11. pp. 1112–1124. With 1 map. English summary. Also in *Rev. Facul de Med.* Bogota. 1941. Nov. Vol. 10. No. 5. pp. 359–376. With 2 maps.

The two previously recognized foci of tick-borne typhus fever in the western hemisphere are—(1) the United States and Canada, (2) Brazil. The disease in Brazil is variously designated by the author as " typhus of São Paulo," " Brazilian rickettsiasis," " spotted rickettsiasis " and " neotropical rickettsiasis." No reference is made in the article to the similar tick-borne fever of Minas Geraes which, presumably, is included in the Brazilian focus.

The author has already described a " spotted fever " in Tobia, Colombia, in 1935. In that outbreak (1934–1936) there were 65 cases with 62 deaths in a population of 267 persons living in a valley just north of the equator at an altitude of 2,300 to 4,100 feet [see this *Bulletin*, 1938, Vol. 35, p. 361].

Two recent cases are described ; they occurred at a place not far from the previous focus. An account is given of the clinical picture of the disease, which resembles the most virulent form of Rocky Mountain spotted fever ; in most of the cases death occurred between the fourth and the tenth day, in the few survivors the fever lasted 14 to 17 days. There were several family outbreaks ; in one of these six members of a family of seven were attacked between June and October 1934 ; in another family one person died in September 1934, five in April 1935, one in May, one in October and one in December of the same year. Two patients recovered from attacks in December, these and a baby were the only survivors in the family.

The people of the affected area and their domestic animals were heavily infested with ectoparasites, and bed bugs, lice, fleas, mites and several kinds of ticks were found.

Four strains of virus were isolated, two from patients, one from ticks found on a patient and one from a mule belonging to a family in which a case had recently occurred. Rickettsia bodies were found in guineapigs inoculated with the virus. Rabbits, *Macacus rhesus* and a local monkey, *Cebus fatuellus*, were also susceptible. The natural vector was *Amblyomma cayennense* : two other local ticks, *Dermacentor*

nitens and *Ornithodorus rudis*, were found to be effective vectors. *D. andersoni*, *O. parkeri* and *O. turicata*, obtained from Montana, were also found capable of transmitting the disease. *Rhipicephalus sanguineus* is mentioned as being common in the area but no reference is made to experiments with this tick.

Sera taken in November 1940, from 16 persons whose histories suggested the possibility that they might have had mild attacks, were sent to Dr. R. R. Parker, who reported that four showed positive protection [presumably against Rocky Mountain spotted fever], eight showed partial or uncertain protection, three were negative, and one was not fully tested. Weil-Felix tests against *Proteus OX19*, *OXK* and *OX2* did not yield positive reactions in dilutions higher than 1–80 in any of the same 16 cases.

Experiments are being carried out in Colombia and Montana to find whether cross-immunity exists between the Colombia strain and the Rocky Mountain strain of the virus. *J. W. D. M.*

Topping (Norman H.). **A Strain of Rocky Mountain Spotted Fever Virus of Low Virulence isolated in the Western United States.**—*Public Health Rep.* 1941. Oct. 17. Vol. 56. No. 42. pp. 2041–2043.

A special strain (designated the "L" strain) of Rickettsiae was isolated from a patient who was infected by a tick, presumed to be *D. andersoni*, in Wyoming. Tested on guineapigs the strain was of low virulence, as shown by a prolonged incubation period, absence of consistent scrotal reaction and a fatality rate of 4·4 per cent. as compared with a rate of 8 per cent., which was the lowest yet recorded in guineapigs inoculated with the mildest strain isolated in the East.

The "L" strain gave complete cross immunity with highly virulent strains of Rocky Mountain fever virus; there was no cross immunity to epidemic and endemic typhus or to strains of Q fever.

The author suggests "that the geographical classification (*i.e.* eastern or western type) be dropped" and that "strains of Rocky Mountain spotted fever should be classified with reference to their virulence to guineapigs."

He points out that there is no justification for the theory that strains of Rickettsiae conveyed by *D. variabilis* are milder than those conveyed by *D. andersoni*. Strains of every degree of virulence are conveyed by ticks of both species.

No mention is made of the duration or severity of the attack in the patient from whose blood the virus was isolated; his temperature was 103·4° two days after the onset. *J. W. D. M.*

Violle (H.) & Joyeux (Ch.). Présence d'un virus à Rickettsias chez des lapins sauvages. [**Rickettsiae found in Wild Rabbits.**]—*Arch. Inst. Pasteur de Tunis*. 1941. June. Vol. 30. No. 1–2. pp. 23–25.

Rickettsiae, assumed to be those of boutonneuse fever, but not identified, were isolated from the pooled blood of five wild rabbits caught in Cardarache, not far from Marseilles. Similar Rickettsiae were recovered from the pooled bodies of a number of ticks (*Rhipicephalus sanguineus*) found on the rabbits.

The blood and the crushed bodies of the ticks were given to rats mixed with their food ; there was a slight febrile reaction in the rats, whose brains were inoculated intraperitoneally into guineapigs. The brains of the guineapigs were inoculated intraperitoneally into rats and Rickettsiae were found in the cells of the peritoneal exudate of the latter animals. No orchitic reaction was observed in the guineapigs, but few males were inoculated.

The brains of the wild rabbits were tested in the same way but no evidence of the presence of the virus was found.

The authors refer to the hypothesis of RAYBAUD (1929) that wild rodents might be reservoirs of the infection of boutonneuse fever in the region of Marseilles, also to the view of DURAND [this *Bulletin*, 1932, Vol. 29, p. 790] and other more recent observers that the dog is the natural reservoir of the virus.

The authors themselves had already shown that the viruses of boutonneuse fever and murine typhus develop and persist in rabbits, the brains of these animals still being infective up to 4½ months. They regard the present experiments as showing that wild rabbits can harbour a virus responsible for the group of endemic typhus fevers of the South of France. *J. W. D. M.*

FINDLAY (G. M.). **Pneumonitis in Mice Infected Intranasally with Q Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1942. Jan. 31. Vol. 35. No. 4. pp. 213–218. With 12 figs. on 3 plates. [17 refs.]

Pulmonary lesions were produced in mice by intranasal instillation of Australian and American strains of the *Rickettsia burneti* of Q fever.

Similar lesions had already been produced in the same way with other Rickettsiae. CASTANEDA (1939), DURAND, GIROUD and SPARROW (1940), and others have reported successful inoculation of mice with the Rickettsiae of murine typhus, exanthematic typhus, Rocky Mountain spotted fever and *fièvre boutonneuse* [see this *Bulletin*, 1940, Vol. 37, pp. 261, 849].

In the present experiment a ten per cent. suspension of the spleens of mice infected with *R. burneti* was used ; four drops of this were instilled into the nostrils of white mice anaesthetized with aether ; for subsequent passages suspensions made from the lungs of infected mice were used in the same way.

The infection was rarely fatal ; mice which were killed four to ten days after infection showed irregularly distributed nodules of consolidation of the lungs, these nodules were associated with terminal bronchi or bronchioles. The chief histological changes in the lungs were as follows :—The bronchi contained a fibrinous deposit and an exudate consisting largely of round cells ; the cells lining the bronchi were prominent but in some places were desquamated. Many of the alveoli were filled with a sero-fibrinous exudate containing few cells, others were almost completely obliterated by swelling of the lining cells and by a heavy infiltration of the interstitial tissues with small lymphocytes and large mononuclear cells. Here and there in the lungs small nodules occurred, they were made up of dense masses of lymphocytes and mononuclear cells with some polymorphonuclear leucocytes and much nuclear débris.

Smears from the lungs showed large numbers of Rickettsiae ; in sections these were seen to be situated in large mononuclear cells on the pleural surface of the lung, in the alveoli, and in the lumen of the bronchi.

The findings resembled those recorded in a fatal human case of laboratory infection with Q fever which occurred at the National Institute of Health in Washington [Lillie *et al.*, this *Bulletin*, 1941, Vol. 38, p. 446].

The author also describes the lesions set up in mice by the intranasal instillation of *R. prowazeki* and *R. murina*; these were usually more intense, but otherwise were essentially similar to those caused by *R. burneti*.

The article is illustrated with excellent photomicrographs.

J. W. D. M.

Cox (Herald R.). **Cultivation of Rickettsiae of the Rocky Mountain Spotted Fever, Typhus and Q Fever Groups in the Embryonic Tissues of Developing Chicks.**—*Science*. 1941. Oct. 31. Vol. 94. No. 2444. pp. 399–403.

The importance and interest of this address* are so great that no apology is needed for giving an exceptionally full abstract.

In 1938 the author reported a simple technique by which the Rickettsiae of Rocky Mountain spotted fever and epidemic typhus could be cultivated in the yolk sacs of developing chick embryos; suspensions of infected yolk sacs were found to be from 100 to 1,000 times more infective than the other tissues of the chick embryos or mammalian tissues. In 1938–39 he showed that cultures grown in the yolk sacs yielded good immunizing vaccines for the Rocky Mountain fever, epidemic typhus, endemic typhus and American Q fever.

The present method of inoculating eggs and maintaining strains is as follows :—

"Fertile eggs incubated for 6 to 7 days at 39°C. are injected in the yolk with infectious material by means of a hypodermic syringe and a 20-gauge needle, 1 to 1½ inches long. The inoculum, consisting of 0·5 to 1·0 cc. of infected, defibrinated guinea pig blood, testicle washings, spleen or brain is introduced through a needle-sized opening in the air-sac end of the egg. After sealing the hole with paraffin, the inoculated egg is incubated at 32°C. in the case of spotted fever, or at 37°C. for typhus or the other rickettsial infections discussed in this paper. Upon death of the embryo, which usually occurs in 3 to 5 days, depending upon the species of rickettsia used, transfer to other fertile eggs is made by means of 0·5 cc. of a 5 to 10 per cent. suspension of yolk sac in a 50–50 mixture of sterile beef infusion broth and saline or by using a like quantity of undiluted yolk fluid. Passage strains can be maintained by either method. Yolk fluid is satisfactory for maintaining strains, but when the tissues are to be used for vaccine production, yolk sac suspension is the preferred inoculum because of its markedly greater infectiveness."

Rickettsiae of all the chief varieties of tick-borne fevers of the typhus group, also of one strain of endemic typhus and one of epidemic typhus, have been cultivated in the same way and studied by the author.

The method has also been used by others for cultivating rickettsial agents, viruses, bacteria and spirochaetes.

In the first few passages the embryo does not die for a relatively long period and maximum multiplication is not usually obtained before 4 to 6 passages, but strains once established can apparently be maintained indefinitely, even in the case of strains which soon die out when transferred through guineapigs.

* Delivered on September 22nd, 1941, to the Section on Medical Sciences upon receipt of the Theobald Smith Award of the American Association for the Advancement of Science.

Rickettsiae from recently established yolk-sac cultures show a notable increase in virulence to guineapigs: the incubation period is shortened, the fever is more intense and the fatality rate is higher. In "orchitic" strains the scrotal reaction is more severe and in "non-orchitic" strains there is often a scrotal reaction. When these virulent strains are passaged through guineapigs they resume their normal virulence after 3 to 4 passages.

The yolk-sac technique is of special value because of its extreme simplicity and the ease with which cultures can be maintained with a minimum risk of contamination.

Preparation and Testing of Vaccines.—Killed vaccines are best prepared from strains of maximum virulence so that the present practice is to use strains that have been carried through a limited number of passages, *e.g.*, "alternated between a series of 40 to 50 yolk passages and several transfers through guineapigs."

The author emphasizes that good vaccines cannot be obtained without using the yolk sac.

The technique now adopted in preparing vaccines is as follows:—

"Upon death of the embryos (in spotted fever this occurs 2 to 3 days, in typhus 4 to 5 days, after inoculation) the pooled embryonic tissues are harvested from all eggs of the same transfer. These are weighed and homogenized to a 12½ per cent. suspension in saline containing 0·5 per cent. phenol and 0·3 per cent. formalin. This suspension is centrifuged at 5,000 r.p.m. for 50 to 60 minutes and the supernatant fluid, which contains the great bulk of lipoids and some soluble proteins, is poured off. The sediment is resuspended with aid of the homogenizer in a volume of saline equal to the original weight of the pooled tissues. Phenol and formalin are added to give a final concentration of 2·0 per cent. and 0·3 per cent., respectively. The resuspended material is placed at room temperature for 6 to 7 days and shaken vigorously daily. During this interval the great bulk of protein is precipitated by the phenol. The suspension is then diluted with 5 volumes of sterile saline and stored at 36°F. for 7 or more days. It is finally centrifuged at 2,500 to 3,000 r.p.m. for 20 minutes, and the resulting supernatant fluid constitutes the vaccine. . . .

"Approximately one liter of vaccine can be prepared from 20 eggs. A bacteriologist and two assistants, provided with proper facilities, can readily prepare from 40 to 50 liters of vaccine per week."

Potency Tests.—The potency of epidemic-typhus vaccine is tested as follows:—

"Twelve guineapigs are used for the potency test, and each receives two 1 cc. injections of vaccine. The test dose for immunity consists of 1 cc. of a lightly centrifuged (1,500 r.p.m. for ten minutes in an International Size 2, horizontal head centrifuge) 5 per cent. suspension of infected brain tissue taken from guinea pigs on the fourth or fifth day of fever. Repeated tests have shown that this inoculum contains 100 to 1,000 infectious doses. Temperatures are taken for 18 days, and 9 of the 12 vaccinated guinea pigs must show complete protection before the vaccine lot is issued.

"Quantitative tests carried out recently with vaccines prepared as described above revealed that guinea pigs can be completely protected against the standard test dose of spotted fever blood virus by giving them as little as 1/16 cc. of vaccine on two occasions. In other experiments it was found that the standard dose of vaccine used in the spotted fever and typhus tests protected guinea pigs in each instance against 100,000 to 1,000,000 infectious units of yolk sac virus. These results certainly indicate a high degree of protection. However, as previously stated, still more potent vaccines can readily be prepared by simply increasing the relative concentration of yolk sac tissue in the final product."

More than 226 litres of typhus vaccine, enough for about 75,000 people, were used in field trials last year. The vaccine was sent to Hungary, Rumania, Spain and China ; the results are not yet known, but there have been no reports of serious reaction even in persons known to be allergic to egg protein. The results are regarded as encouraging.

Formalinized suspensions of Rickettsiae of Q fever and epidemic typhus have been prepared and are stable in storage and agglutinable by specific antisera.

Studies are now in progress to determine the availability of rickettsial suspensions for diagnostic skin tests.

A strain of Rocky Mountain fever Rickettsiae of low virulence has been maintained in eggs for 240 serial transfers : yolk-sac suspensions of the 11th and 15th passages were highly virulent for guineapigs, but from the 50th to the 125th passages the suspensions became markedly less virulent and many inapparent immunizing infections were observed.

For the subsequent 100 passages the strain showed a consistently low degree of virulence to guineapigs, but even when no reaction of any kind was apparent the animals were found to be solidly immune to massive doses of highly virulent strains. If it should turn out that a high and lasting immunity is caused by the avirulent strain it may eventually be possible to immunize man with modified living strains of Rickettsiae in much the same way as they are now being immunized against yellow fever. *J. W. D. M.*

Nauck (E. G.) & Weyer (F.). Versuche zur Züchtung von Rickettsien in explantiertem Läusegewebe. [**Experiments in the Growth of Rickettsiae on Tissue-Culture Media made from Lice.**]—*Zent. f. Bakt.* I. Abt. Orig. 1941. Aug. 28. Vol. 147. No. 6. pp. 365–376. With 4 figs. [10 refs.]

A full account is given of the use of culture media containing tissues of lice, bugs and fleas. Tissues derived from the larvae of lice were found to be the most satisfactory ; they kept in good condition for several weeks without showing any multiplication of the tissue cells. Various kinds of Rickettsiae grew profusely, especially in stomach tissues. *R. prowazeki* multiplied only when it had already been present in the lice before the removal of the tissues. Lice inoculated *per anum* with the tissue cultures showed only extracellular Rickettsiae and these were neither infective to guineapigs nor capable of being grown in subcultures. *J. W. D. M.*

i. Findlay (G. M.). **Relationship of Exanthematic and Endemic Typhus.**—*Lancet.* 1941. Nov. 29. pp. 659–660. [12 refs.]

ii. Lancet. 1941. Nov. 29. p. 671.—**Typhus Immunisation.**

i. Findlay begins with a brief review of the evidence in support of the existence of cross immunity between endemic and exanthematic typhus. He states that murine killed vaccine protects guineapigs against the virus of exanthematic typhus, the degree of immunity depending on the dose of the vaccine ; but little is known about the efficacy of inoculation of human beings with Rickettsiae.

In January 1940 Findlay himself, aged 47, received three injections of Weigl's louse vaccine : there was no reaction and no evidence of the presence of immune bodies was found, either in the form of a positive Weil-Felix reaction or a positive response to Giroud's intradermal test in rabbits.

In April 1940 he had four injections at five-daily intervals of a mouse-lung vaccine prepared by DURAND and GIROUD : this was a killed vaccine made from the Rickettsiae of epidemic typhus. The Giroud test showed that immune bodies were present.

In June 1940 while working with Rickettsiae of exanthematic and endemic typhus he had a mild attack of fever lasting five days with a maximum temperature of 101°F. ; an orchitic strain of typhus Rickettsiae was isolated from his blood taken on the 2nd day of the fever.

A laboratory technician, aged 18, received an injection of mouse-lung vaccine made from killed Rickettsiae of epidemic typhus ; five days later he had a second dose ; one day after this he was attacked by fever which lasted a fortnight with a maximum temperature of 103·8°F.

An orchitic strain of Rickettsiae was isolated from his blood.

Findlay's attack was apparently modified by immunity resulting from the previous inoculations.

The " unrehearsed human experiment therefore bears out the contention that there is a close antigenic similarity between rickettsiae of exanthematic and endemic typhus " and that the relationship between these is " quantitative rather than qualitative."

ii. Methods of typhus immunization are briefly reviewed in an editorial article which has obviously been written by a competent authority on the subject. A commendably conservative attitude is maintained, as is shown by the remark that " little is yet known about typhus immunization on a large scale."

Weigl's killed louse-vaccine has been in use for a considerable time : some hundreds of lice are needed for the immunization of a single person, the technique is delicate and numbers of immune persons must be available to provide nourishment for the thousands of lice that have to be fed. For large-scale preparation of the vaccine a whole institute is necessary.

Immunization on a large scale has been carried out in Morocco and Tunis by the injection of living murine virus ; immunity is often acquired at the expense of an attack of murine typhus which, though not so dangerous as epidemic typhus " is not to be despised." Another drawback is that in louse-infested communities there is a possibility of the strain being converted to one of epidemic typhus by passage through lice.

Killed vaccines prepared by the methods of Cox and of Durand and Giroud have been employed, but hitherto on a small scale ; they necessitate four or five injections and their actual value in the field is not yet known.

The duration of immunity resulting from killed vaccines is probably not more than a year. Immunity should be tested not only by the Weil-Felix reaction but also by the agglutination test [presumably with Rickettsiae] and by Giroud's intradermal test in rabbits.

Both Weigl's vaccine and mouse lung vaccine lose much of their antigenic power after 5–6 months, even when kept in the ice-chest.

J. W. D. M.

EYER (H.), PRZYBYLKIEWICZ (Z.) & DILLENBERG (H.). Das Fleckfieber bei Schutzgeimpften. [**Typhus Fever after Protective Inoculation.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1940. Nov. 22. Vol. 122. No. 6. pp. 702–719. With 15 figs.

Fifteen cases of laboratory infection with typhus fever occurred among the personnel of a German Military Institute in Cracow where Weigl's vaccine was being prepared from artificially infected lice. The onset in 8 cases was between the 8th and 28th May, 1940, in 6 it was in June, and in 1 in July.

In three cases the infection must have been conveyed by the bites of infected lice which were being fed on the patients for 9, 13 and 15 days respectively before the onset of the attacks. These three cases were of 12 to 13 days' duration and were rather severe although the patients had been inoculated with Weigl's original vaccine on two occasions within the previous four months.

In another case the source of infection was something of a mystery, the patient had been engaged in supplying blood feeds to infected lice for two months before the onset, but also had been handling the faeces of infected lice : his attack was the longest (15 days) and most severe of those recorded. He had been inoculated twice with Weigl's vaccine.

The remaining 11 cases ranged in duration from 5 to 10 days ; the patients had not been bitten by infected lice but were engaged in preparing vaccine and so must have been infected with the dried faeces of lice. Seven of the patients had been inoculated on one occasion with Weigl's original vaccine within the previous five months, three had been twice inoculated, and one had been inoculated six months previously and also had an attack of typhus fever two months before the onset. The three patients who had been twice inoculated and the one who had a previous attack escaped with exceptionally mild attacks lasting five to eight days.

In view of the very heavy doses of infection that must have been received the author concludes that the vaccine had conferred a considerable degree of immunity, which would probably have been sufficient to prevent recognizable attacks of typhus in persons infected in the usual way. He holds that the efficacy of the vaccine has been thoroughly established by the results of large-scale trials in the field.

The serum-agglutination test with suspensions of Rickettsiae was found to be more specific than the Weil-Felix reaction : it became positive at an earlier stage and also became negative sooner after the fall of the temperature. This reaction, known as Weigl's R.A. test, is regarded as diagnostic when it is positive in titres of 1–50 and over ; the Weil-Felix reaction is diagnostic in dilutions of 1–100 to 1–200 and over. *J. W. D. M.*

MED. WELT. 1942. Jan. 3. No. 1. p. 26. **Limited Possibilities of Typhus Vaccination.**

At a meeting of the Berlin Medical Society, GELLMEISTER reported that the Weigl vaccine against typhus fever made from the louse gut cannot be produced in sufficient quantities. The new vaccine of Otto-Gellmeister-Hagen is easy to produce, but has not yet been proved in the field. It appears that it will never be possible to carry out protective inoculation against typhus in the same extensive

manner as can be done for typhoid. Only those persons specially exposed to the danger of infection should be vaccinated.

W. P. Kennedy.

Pechtel (C.). Eubasin-Effekt bei einem Fall von Wolhynischem Fünftagefieber. [**The Effect of Eubasin (Sulphapyridine) in a Case of Wolhynian Five-Day Fever (Trench Fever).**]—*Med. Klin.* 1940. Nov. 29. Vol. 36. No. 48. p. 1331. With 1 chart.

The patient had been engaged on harvest work in the company of a Pole. The fever was of an irregular relapsing type in which the periodicity varied between three and five days. The symptoms corresponded to those described in trench fever and had persisted for two months before admission to hospital. After admission to hospital there were five further spells of fever on the 1st, 6th, 9th, 14th and 17th days respectively.

The serum agglutinated *Proteus X19* up to a titre of 1–160.

Sulphapyridine treatment was started two days after the last paroxysm of fever, 15 grammes were given in four days. The symptoms yielded promptly and there was no return of the fever.

J. W. D. M.

Peña Yañez (A.). Ueber den Einfluss von Antimonsalzen auf das Fünftagefieber [**The Use of Antimony Salts in Trench Fever.**]—*Deut. Med. Woch.* 1941. Nov. 14. Vol. 67. No. 46. pp. 1267–1268. With 3 charts.

The author treated eight cases of trench fever, during the Spanish civil war, by means of tartar emetic, with good results. The doses used were from 8 to 14 cc. of a 1 per cent. solution, given intravenously each day for seven days, and if necessary repeated after an interval of a week. Diagnosis was made on the typical temperature curve. Charts of three patients are shown; in two a single course of the drug sufficed for cure, in the third there was a slight recrudescence which yielded to a second course.

C. W.

Howe (Calderon). **Demonstration of Agglutinins for** *Bartonella bacilliformis.*—*Jl. Experim. Med.* 1942. Jan. 1. Vol. 75. No. 1. pp. 65–75. With 2 figs. [10 refs.]

A satisfactory agglutination test for bartonellosis (Carrión's disease) is now available for the first time. Hitherto it has been impossible to prepare suitable suspensions of *Bartonella bacilliformis*, but two media devised by Geiman (*Proc. Soc. Experim. Biol. & Med.*, 1941, Vol. 47, p. 329), yield cultures from which homogeneous suspensions can be obtained. Details of these media and of the method of preparing the suspensions are given. [See also this *Bulletin*, 1942, Vol. 39, p. 156.]

By repeated intravenous injections of live cultures of *B. bacilliformis* into rabbits a strongly agglutinating serum can be obtained. The sera of five immunized animals gave positive reactions in titres of 1–160 to 1–640. Sera from six patients in various stages of bartonellosis also agglutinated the organisms, but at much lower titres, ranging from 1–10 to 1–80. These reactions were significant because 13 control sera of healthy persons showed no agglutinins.

The six positive sera were also tested against *Proteus OX19, OXK* and *OX2*. Some of these sera showed significant amounts of agglutinins against all three organisms ; three reacted in titres of at least 1–64 to *OX19*, one to *OXK* and three to *OX2*. No conclusions could be drawn from these reactions but the highly immunized guineapigs gave entirely negative reactions to all the Proteus organisms.

J. W. D. M.

MALARIA.

Fellows (Frank S.) & Perry (William B.) **Syphilis-Malaria Survey, Onslow County, North Carolina.**—*Venereal Dis. Information.* 1941. July. Vol. 22. No. 7. pp. 237–247. With 2 figs. [Summary appears also in *Bulletin of Hygiene.*]

Various surveys carried out in N. Carolina have differed in their estimates of the amount of syphilis and malaria there. That under review, which was conducted in Onslow County from August 1939 to April 1940, was to determine not only the prevalence of syphilis and malaria there but also the effect of malaria on the syphilitic serum reactions. Onslow County was chosen as one in which hitherto little anti-malarial or anti-syphilitic work had been organized. Its population in 1930 was 15,289, and of these 26·6 per cent. were negroes ; the survey was conducted entirely amongst the negroes, of whom 80 per cent. were tested by serological tests of venous blood and microscopical examination of thick films of finger blood. Positive and doubtful results led to re-tests, and eventually it was decided that 9·9 per cent. gave positive reactions to syphilis tests and 5·0 per cent. doubtful. These results show a lower prevalence of syphilis in negroes than in some similar communities elsewhere, *e.g.*, Tennessee and Georgia each with 26 per cent., though the percentage in Mississippi was 7·1 and in Virginia 9·7. In Onslow County the percentage varied with different districts from 0 to 23. The generally low prevalence may be due to the fact that the population is very stable, and there is no evidence of any great influx from outside. Analysis by marital status showed the highest prevalence in the separated group and next in the married and widowed ; 17·2 per cent. of housewives were infected. Amongst many points illustrated in the ten tables it appeared that 81·3 per cent. of the positive cases had had no previous treatment. The histories showed that 16 had been found positive within a year before the survey but only four cases of syphilis had been notified to the health authority. In women over 20, those with syphilis had had an average of 3·5 pregnancies each as compared with 4·4 in the non-syphilitic group. Of the syphilitic women aged over 20, 81 per cent. had conceived as compared with 85 per cent. of the negative reactors, " probably," the authors say, " showing a higher sterility rate in the syphilitic woman." In those who had conceived, the syphilitic women had an average of 4·3 pregnancies each as compared with 5·2 in the non-syphilitic.

Malarial parasites were found in 3·1 per cent. of the 3,244 negroes so examined, and the commonest parasite was *P. falciparum* (93·1 per cent.). Malaria has been notifiable since 1937, but although the authors estimate that 200 cases must have been treated for it in the year before the survey, only five had been reported from the beginning ;

eight deaths had occurred since 1937. Of the persons in whom malarial parasites were found, 77 per cent. were under 20, 72 per cent. being of pre-school or school age. Details are given of both malaria and syphilis by districts and occupational status. As regards the question of the influence of malaria on the syphilitic serum reaction, it is noted that 10·9 per cent. of the malarial group (with parasites) had positive serum reactions and 23·8 per cent. doubtful, which compares with 7·5 and 5·6 respectively in the non-malarial. In the group with malarial parasites in the blood 64·8 per cent. of those who gave a positive or doubtful reaction with the first syphilitic serum test showed a change in the reaction with subsequent tests, 5·4 per cent. from positive to doubtful, 27 per cent. positive to negative, 29·7 per cent. doubtful to negative and 2·7 per cent. doubtful to positive. In contrast with this, only 24·9 per cent. of the non-malarial group giving positive syphilis reactions showed any change on subsequent testing. The authors discuss also reasons for those giving a history of malaria giving a higher percentage of positive syphilis reactions than those with no such history and suggest that natural malaria may cause false positive reactions for longer than the 66 days which KITCHEN *et al.* showed them to persist after disappearance of parasites following therapeutic malaria. *L. W. Harrison.*

FAUST (Ernest Carroll). **Malaria Mortality in the Southern United States for the Year 1939 with Notes on Malaria in Other States.**—*Southern Med. Jl.* 1941. July. Vol. 34. No. 7. pp. 708–709.

" In all of the United States except the South, endemic malaria transmitted by mosquitoes is due to *Plasmodium vivax*. Imported cases from the South or tropical America frequently harbor *Plasmodium falciparum*.

Summary.

" Malaria mortality in the Southern United States for the year 1939 was apparently the lowest on record ; it was 20 per cent. lower than for 1938 and 30 per cent. lower than the previous low of the 5–7 year cycle of malaria mortality. In the relatively few counties in the South with significant increase in malaria deaths in 1939 over 1938 there is suggestive evidence of radial distribution of the infection from near-by highly endemic foci. Outside the South, Illinois is the only state with a significant number of malaria deaths during the past three years. However, many of the Northern and Western states have indigenous malaria. In Iowa, Illinois, Wisconsin and southern Minnesota mild epidemics developed in Counties near the Mississippi River during the summers of 1938 and 1939. Moreover, transient laborers, CCC camp enrollees, tourists returning from the South and tropical America, as well as patients with malaria who are sent to the North and West to recuperate, all constitute increasing sources for introducing the infection into previously non-malarious localities."

YAO (Y. T.) & WU (C. C.). **On the Peculiar Morphology of the Malaria Parasite from a Patient and the Possibility of its being *Plasmodium ovale*.**—*Chinese Med. Jl.* 1941. Aug. Vol. 60. No. 2. pp. 178–183. With 4 plates (2 coloured).

A patient, aged 21, was admitted to Kun Hua Provincial Hospital, Kunming, China, suffering from fever associated with the presence in

the blood of *Plasmodium falciparum* (rings and crescents) and of another malarial parasite which appeared to exhibit all the features of *P. ovale*. The patient on admission was acutely ill but quickly responded to treatment with quinine, atebrin and plasmoquine. The illness was not of such severity that growing forms and schizonts of *P. falciparum* would be present in the peripheral blood. This would exclude the possibility that the parasites assumed to be *P. ovale* could be stages of *P. falciparum*. The *P. ovale*-like forms included all stages of development, from rings to mature schizonts and gametocytes, which are illustrated in a coloured plate and two plates of microphotographs. The main features are stippling of infected cells, oval shape of parasite and cells, many of which have frayed edges, failure of cells to enlarge, mature parasites, schizonts and gametocytes not completely filling the cells, number of merozoites 8 to 12. All these features are consistent with a diagnosis of *P. ovale*. The authors are guarded in their final conclusion, which is that there is the possibility of the presence of *P. ovale* in China. *C. M. Wenyon.*

Bates (M.). **Field Studies of the Anopheline Mosquitoes of Albania.**—*Proc. Ent. Soc. Wash.* 1941. Vol. 43. No. 3. pp. 37–58. With 7 figs. [15 refs.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1942. Feb. Vol. 30. Pt. 2. pp. 29–30.]

Field observations on the Anophelines of Albania, made between 1936 and 1939 in connection with the programme of the laboratory for mosquito research in Tirana, are summarised. Those found comprised *Anopheles algeriensis*, Theo., *A. claviger*, Mg., *A. hyrcanus* Pall. (possibly subsp. *pseudopictus*, Grassi), *A. marteri*, Senevet and Prunelle, *A. plumbeus*, Steph., *A. superpictus*, Grassi, and four members of the group of *A. maculipennis*, Mg. (vars. *messeae*, Flni., *sacharovi*, Favr., *subalpinus*, Hackett and Lewis, and *typicus*) for which the author adopts the nomenclature he proposed in a recent paper. Brief notes are given on their local distribution and also keys for the identification of the eggs and fourth-instar larvae. The larvae of the *maculipennis* group can in most cases be identified by means of the variation in the antepalmate hairs, and a table is given to show how this method of identification is applied to field material.

As in Greek Macedonia, intense malaria in Albania is associated with *Anopheles maculipennis* var. *sacharovi*, but the disease also occurs in areas where this form is not found, and it then appears to be carried by *A. superpictus*. It is also found in a few places, notably on the shores of Lake Malik, where the only common mosquitos are *A. maculipennis* vars. *typicus*, *messeae* and *subalpinus*, which are generally supposed not to be vectors because they do not readily attack man. The villages are very near the lake where the mosquitos breed in immense numbers.

Larval habitats were studied in detail only for the members of the *maculipennis* group. Of these, var. *subalpinus*, which occurred all over the country but bred only in marshes and ponds, has the most limited habitat. It was never found in heavily shaded situations, in water with a small surface area, high nitrate content or appreciable salinity or in water free from vegetation or subject to strong surface movements. The limitations of var. *messeae* were similar, and moreover, its geographical range in Albania is very limited, possibly

because of the effect of the maximum summer temperature on the adults. Var. *sacharovi*, though typically a marsh breeder, was found in small bodies of water, such as pools and ditches, and in water containing slightly more than 2 per cent. sodium chloride, but is subject to the other limitations. The geographical range of this form also is limited, possibly through the effect of minimum winter temperatures on the adult. Var. *typicus* was found all over Albania in a wide range of habitats, but in general the limitations were the same as those for *subalpinus* except for that of area of water surface. *A. superpictus*, which breeds typically in the small pools in gravelly river beds, is thus not subject to the limitations of vegetation and surface movement. Late in the season, when the adult population has reached its maximum, the eggs may sometimes be found in very varied habitats, including small pools and rice-fields. *A. hyrcanus* and *A. algeriensis* were most abundant in a large marsh. Larvae of *A. plumbeus* were found only in tree holes. In the summer, *A. claviger* was found only in shaded spring-fed pools, but in the winter and early spring, it occurred in many types of habitat. The pools in mountain streams in which *A. marteri* bred were characterised by heavy shade, low temperature and clear fresh water. The field study of the eggs was found to be the most useful way of defining the breeding places of the various members of the *maculipennis* group. The author believes, therefore, that the ecological distribution of Anophelines depends on selection of the oviposition site by the female.

The seasonal distribution of adults of var. *typicus* as previously determined was compared with larval distribution. The decline in the numbers of adults during July was first attributed to the fact that many of the breeding places near Tirana, where the survey was made, dry up at this time. However, when in 1937 a small permanent stream was dammed to form a shallow pool that could be kept at a constant level throughout the summer, the larval population in the pool declined at a similar rate to the adult population, beginning slightly earlier, and there was no great increase in the number of first-instar larvae after the peak in the adult population. These results were thought to indicate that the drop in population is largely due to a high mortality of adults, probably on account of high temperature and low humidity. In each of the years 1933–37, the peak of the population preceded the peak in mean temperature. The technique used for counting the larvae is described.

Data on the relative numbers of larvae in different instars were collected for various breeding places and seasons on the theory that the ratio between instars might be fairly constant during the period of continuous breeding and that variation in it might throw light on seasonal changes of population. Ratios are given for larvae from five breeding places of var. *typicus* in Albania, in two of which vars. *messeae* and *subalpinus* also occurred, and for var. *atroparvus*, van Thiel, in Portugal according to Cambournac. The ratio in var. *typicus* varied considerably from one breeding place to another and would even appear to be more useful as an index of differences between breeding places than in the study of seasonal variation. On the basis of observations on the duration of the various instars of var. *atroparvus* when reared in a favourable medium, which are discussed, the percentage of larvae in the four instars in an area of continuous breeding with no mortality should be 16, 20, 24, and 40, respectively. In the natural breeding places, these ratios were, with one exception, more or less

reversed, the greatest number of larvae being in the first instar, and this suggests an interesting approach to some of the problems of larval ecology.

[See also this *Bulletin*, 1941, Vol. 38, p. 558.]

Russell (Paul F.) & Mohan (Badri Nath). **Experimental Malaria Infections in *A. stephensi* from Contrasting Sea-Water and Tap-Water Larva Environments.**—*Amer. Jl. Trop. Med.* 1941. July. Vol. 21. No. 4. pp. 553–558. [11 refs.]

The authors have previously published reports which show that the chemical character of the water in which *A. stephensi* breeds has little or no influence on the susceptibility of adults to infection with *P. falciparum* [see this *Bulletin*, 1940, Vol. 37, p. 359]. This is a continuation of that work. Starting with ova from tap-water colonies the authors were gradually able to establish colonies in water containing as much as 80 per cent. sea water. It is interesting to note that the larvae of *A. stephensi* developing in high concentrations of sea water showed marked shortening of the anal papillae.

A total of 260 adult *A. stephensi* from tap-water and 330 from sea-water larval environments were fed on gametocyte carriers, in eight lots. In one lot all the mosquitoes failed to become infected. The sporozoite indices in the remaining 221 tap water and 298 sea water *A. stephensi* were 27·1 and 31·9 per cent. respectively, the highest sporozoite indices in any single lot being 71·2 and 81·6 per cent. respectively. Once more it is shown that chemical changes of larval environment do not modify the capacity of emerging *A. stephensi* to transmit *P. falciparum*. *Norman White.*

Brambilla (Alberto). L'anofelismo nella zona di Dire Daua (Harar). Prima nota. [**Anopheline Prevalence in the Dirre Daua Region (Harar).**]—*Riv. di Malariologia*. Sez. I. 1941. July–Aug. Vol. 20. No. 4. pp. 271–293. With 20 figs. English summary (7 lines).

In a previous communication the author dealt with malaria prevalence and anophelines in Dirre Daua [this *Bulletin*, 1941, Vol. 38, p. 709]. He now reports the results of an anopheline survey carried out during 1939 in the country surrounding Dirre Daua, within a radius of about 100 kilometres. Twenty photographs of Anopheles breeding places illustrate the text. The report does not lend itself to summary.

Eight species of Anopheles were found. *A. gambiae* was most prevalent. Others in order of prevalence were *A. d'thali*, *A. pretoriensis*, *A. cinereus*, *A. turkhudi*, *A. demeilloni*, *A. garnhami*, and *A. rhodesiensis*. *N. W.*

Hopkins (G. H. E.). **The Range of Flight of Anopheline Mosquitoes.**—*East African Med. Jl.* 1941. Sept. Vol. 18. No. 6. pp. 175–183.

A very high incidence of malaria among staff and pupils at Busoga College situated on the summit of Mwiri, an isolated hill two miles to the north of Lake Victoria, led to an investigation of the source of the mosquitoes concerned. Fairly large numbers of *Anopheles funestus* were found in the College and no breeding places could be discovered nearer than the swamps along the lake-shore two miles away, where

breeding was exceedingly prolific. Observations on the wind showed that this regularly blows from the lake until about 11 p.m. These factors of wind and abundance of mosquitoes were clearly responsible for extending the " effective range " of *funestus* up to two miles in this locality. But the author holds that in most localities half a mile will give adequate protection against this species ; maintaining that it is " better to control thoroughly a small area than to dissipate our energies by attempting partial control over a larger area."

V. B. Wigglesworth.

Smith (Gordon E.), Watson (Robert Briggs) & Crowell (Robert L.). **Observations on the Flight Range of** *Anopheles quadrimaculatus*, **Say.**—*Amer. Jl. Hyg.* 1941. Sept. Vol. 34. No. 2. Sect. C. pp. 102–113. With 2 figs.

The authors discuss some observations on the range of flight of *Anopheles quadrimaculatus* in Tennessee.

They stained 3,800 mosquitoes of this species and liberated them at one spot in the course of two months. Only six were recovered, all between 130–900 yards from the point of liberation. Certain field observations are recorded on the proximity of places where adults could be collected to breeding sites : also on the distribution of malaria in houses at different distances from the lakeside. All the work is consistent with what is already known about this species elsewhere in the U.S.A., for there is a considerable body of evidence that it never ranges very far, though flights up to 1½ miles have been recorded. [It is interesting to contrast the range of flight of this insect with the much greater range of the very similar *Anopheles maculipennis* in Mediterranean countries.]

The paper contains nothing to indicate whether *Anopheles quadrimaculatus* flies much greater distances in the autumn before it commences to hibernate. *P. A. Buxton.*

Boyd (Mark F.). **On the Temperature of Incubation for Anophelines infected with** *Plasmodium falciparum.*—*Amer. Jl. Trop. Med.* 1941. Sept. Vol. 21. No. 5. pp. 689–694.

If Anopheles are infected with *Plasmodium falciparum* and kept at 20°C. one obtains a lower proportion of infections and a smaller number of oöcysts than if one incubates mosquitoes infected with *P. vivax* at the same temperature.

It is found that (using *Anopheles quadrimaculatus*), at 28°C. the number of oöcysts obtained is higher than at 20°C., though the percentage of mosquitoes infected is about 62 at each temperature. At the higher temperature sporozoites are first found on 9th–15th day, at the lower on 19th–24th. *P. A. B.*

Quattrin (Nevio). Ricerche sull'inoculazione del parassita malarico per via intramidollare. [**Intramedullary Inoculation of Malaria Parasites.**]—*Riv. di Malariologia.* Sez. I. 1941. July–Aug. Vol. 20. No. 4. pp. 229–237. French summary.

Nine patients requiring malaria therapy were the subjects of the experiments described in this paper. Sternal punctures were performed and infected blood from malaria patients was injected into the sternal medulla. The blood was taken from patients, who had been

infected with *P. vivax*, either intravenously or intramuscularly, during their fifth or sixth febrile attack, a period in which, in the experience of the author, the peripheral blood has maximum infectivity. The amount of blood so injected was from 3 to 8 c.c. At intervals of from 10 to 180 minutes after the injection specimens of bone marrow were taken for microscopic examination. It was found that infected blood disappears from the sternal bone marrow very rapidly. Parasites were found only three times in 22 very prolonged examinations of marrow preparations. These positive findings were in preparations made 15, 40 and 70 minutes after the inoculations. These rare parasites showed no abnormality of structure or staining reaction, or relationship to the red cells which sheltered them. No parasites were ever found either in myeloid cells or in reticulo-endothelial cells.

Three of the 9 patients failed to give any clinical evidence of infection in spite of having received 6, 7 and 8 cc. respectively of heavily infected blood. The incubation period in four of the six successfully infected patients was 8 days ; in the remaining two patients it was 6 days and 12 days respectively. The incubation period with intravenous inoculation of similar infected blood has generally been, in the author's experience, from 3 to 4 days. *N. W.*

Southwell-Sander (G.) & Hand (R. F.). **Observations on Some Cases of Malaria.**—*Jl. Roy. Nav. Med. Serv.* 1941. July. Vol. 27. No. 3. pp. 300–307.

This paper gives detailed accounts of seven cases of malaria, all of which presented interesting features. In one the authors were fully justified in making a diagnosis of acute malaria in spite of the fact that at no time were parasites discoverable in the peripheral blood. In two cases of pernicious malaria and in one which gave rise to symptoms of blackwater fever the paucity of parasites in the peripheral blood afforded no indication of the severity of the infections. In one case the symptoms and signs at the onset simulated those of pneumonia : in another those of a severe streptococcus septicaemia. In these, treatment with sulphonamides produced improvement, but a cure was not effected until the malaria infections were discovered and antimalaria therapy instituted.

In nearly all the cases there was a rise in the sedimentation rate. In two cases this was noted about a week after the onset of clinical symptoms. The rate falls to normal after adequate treatment. One case suggests that the persistence of a high sedimentation rate after treatment may indicate the persistence of infection and the probability of a relapse. *N. W.*

Still (R. M. Lloyd) & Lal (T. N.). **A Case of Cerebral Malaria with Rare Complications and Complete Recovery.**—*Indian Med. Gaz.* 1941. July. Vol. 76. No. 7. pp. 418–419.

The patient, a Punjabi woman of 18, was admitted to hospital with pyrexia and developing coma ; rings of *P. falciparum* were found in the blood. She was given intravenous quinine but became fully comatose. The next day the temperature was lower and the patient regained consciousness but was unable to speak, and the aphasia persisted. On the fifth day hemiplegia of the right side developed though the temperature was normal. Anti-malaria treatment had been given

continuously and was now combined with iodides and massage, and the patient regained the use of her leg in about a fortnight. Speech and the use of the arm came back gradually, and the patient was discharged cured after about six weeks. The malaria infection was never heavy. *C. W.*

KUTSCHERA-AICHBERGEN (Hans). Sepsis mit malaria-ähnlichem Fieberverlauf. [**Sepsis with a Febrile Course simulating Malaria.**]—*Wien. Klin. Woch.* 1941. Aug. 8. Vol. 54. No. 32. pp. 666–667. With 1 chart.

Two cases are recorded in which the febrile course was strongly suggestive of malaria. In both cases a diagnosis of gonococcal septicaemia was made on the strength of a positive Müller-Oppenheim reaction, but without any other evidence of gonococcal infection.

Both of the patients were treated with albucid (a sulphonamide preparation). In one case, after a month's illness a complete cure was effected by four intravenous injections of the drug, given in doses of 10 cc. daily.

The other case is reported in detail: the attack began suddenly with high fever; by the fourth day there was pain and swelling of one knee joint. After six days' treatment with salicylates the fever and swelling subsided.

About a fortnight later the fever returned, for two weeks the temperature chart showed a quartan periodicity, then for a week it was tertian.

Although no parasites were found, quinine was given for five days and the fever became of an irregular quotidian type. Eight days after the end of the course of quinine the temperature became higher than ever and was again tertian in type: the fever yielded promptly, but temporarily, to albucid, of which 63 tablets were given in six days. Two days after the end of the course of albucid the temperature rose again and there were two paroxysms with tertian periodicity. The fever again yielded to albucid and the temperature remained subnormal for five days, but within two days of the end of the second course of the drug the temperature rose again and high remittent fever continued till the death of the patient four days later.

The post-mortem examination showed endocarditis with disorganization of the left aortic valve, from which cultures of pneumococci were obtained. These organisms were regarded as secondary invaders in a case which was primarily one of gonococcal septicaemia.

The author refers to six recorded cases of non-malarial tertian or quartan fever: in only one of these was the cause found—a meningococcus. He also mentions that French observers 40 years ago described a "fièvre pseudopalustre gonococcémique" (pseudo-malarial fever due to gonococcal septicaemia). *John W. D. Megaw.*

AKASHI (Kazuyoshi) & SO (Teiju). **A Simple Sero-Diagnostic Method for Malaria.**—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1941. July. Vol. 40. No. 7. [In Japanese pp. 1292–1300. [17 refs.] English summary p. 1301.]

The test is performed as follows—0·2 cc. serum from the patient is mixed with 1·0 cc. distilled water made faintly alkaline to phenol phthalein, and 0·1 cc. of 0·5 per cent. formalin. The mixture is

shaken and allowed to stand at room temperature for 2 hours. A flaky appearance on examination with a lens indicates a positive result.

In malaria the test is always positive after 3 or 4 days from the onset and is especially pronounced in chronic cases in which treatment has not been adequate ; it becomes negative a month or two after cure. It is also strongly positive in certain forms of jaundice, hepatic cirrhosis, eruptive fevers, measles and kala azar, and slightly positive in certain cases of splenomegaly, pernicious anaemia, leukaemia, typhoid, rheumatic arthritis, malignancy and in cases of the Wassermann positive diseases. These, it is claimed, are easily differentiated from malaria. There appears to be an increase of serum euglobulin in positive cases ; the test is a variant of the Henry test. *C. W.*

Coggeshall (L. T.), Maier (John) & Best (C. A.). **The Effectiveness of Two New Types of Chemotherapeutic Agents in Malaria : Sodium P,P′-Diaminodiphenylsulfone N,N′-Didextrosesulfonate (Promin) and 2-Sulfanilamido Pyrimidine (Sulfadiazine).**—*Jl. Amer. Med. Assoc.* 1941. Sept. 27. Vol. 117. No. 13. pp. 1077–1081. With 5 charts. [Refs. in footnotes.]

This is a contribution to the search for more effective antimalaria remedies than any yet known. Coggeshall has already shown that sulphanilamide is capable of eradicating *P. knowlesi* infections in rhesus monkeys, but that it has little or no effect on human *P. vivax* infections or on *P. lophurae* and *P. cathemerium* infections in birds [this *Bulletin*, 1939, Vol. 36, p. 824]. Attempts are being made to find some related substance that may have an action on human infections similar to that of sulphanilamide on *P. knowlesi* infections in monkeys. The present paper deals with promin and sulphadiazine, the chemical constitutions of which are set out in the title above.

Promin was found to be as effective as sulphanilamide or its derivatives against *P. knowlesi*, *P. cynomolgi* and *P. inui* infections in rhesus monkeys. Next it was shown that promin possesses definite antimalaria activity against induced *P. vivax* infections : five patients undergoing malaria therapy were the subjects of this part of the inquiry. Finally, 17 patients suffering from naturally acquired malaria were treated with promin at the Gorgas Hospital : eight of these were negroes, nine were white residents. Five were *P. falciparum* infections, 12 *P. vivax*. The dosage of the drug varied from 10 gm. to 40 gm. a day, intravenously, for not more than four days [this seems to be an enormous dose, but is correct according to the original]. It is pointed out that 1 gm. of promin contains only 0·31 gm. of active agent, the remainder being the inactive dextrose-sodium sulphonate radical. Toxic reactions to the drug were minimal ; two patients had a moderate degree of cyanosis which disappeared when the drug was discontinued. The drug is excreted extremely rapidly. Promin had a definite action on both forms of parasite but *P. vivax* was more resistant than *P. falciparum*. Infections in negroes were more responsive than infections in the relatively non-immune white patients.

Sulphadiazine was used in the treatment of 13 negroes suffering from naturally acquired acute malaria, seven *P. vivax*, five *P. falciparum* and one *P. malariae* infections. The dosage was 6 gm. the first day and 4 gm. daily for the next five days : it was given by mouth at four-hourly intervals during the day-time. In three patients, two

with *P. falciparum* and one *P. vivax* infection, the drug was of no avail: in the remainder fever and parasites disappeared during the treatment.

The authors conclude that there are no reasons for giving either promin or sulphadiazine in preference to quinine or atebrin for the treatment of malaria, but both may be looked on as important substitutes.

N. W.

Rose. Malariaprophylaxe mit Atebrin, ihre Dosierung und angeblichen Komplikationen. [**Malaria Prophylaxis with Atebrin; Dosage and Alleged Complications.**]—*Deut. Med. Woch.* 1941. Nov. 28. Vol. 67. No. 48. pp. 1306–1308.

Rose is unequivocally in favour of the daily administration of atebrin, if only because administration of larger doses once or twice each week is apt to be forgotten in military communities. He advocates a daily prophylactic dose of 0·06 gm., and has had tablets of this strength prepared, but cannot as yet give definite figures of results obtained. The dose is, however, higher than that often used (0·05 gm.).

This method of prophylaxis was used during the Balkan campaign of the present war and the drug was alleged, by some of the men and doctors alike, to have a cathartic action. Rose points out, however, that in the Mediterranean area dysentery of the Flexner type, and milder forms of diarrhoea, are not uncommon, and that it is to these infections that the symptoms attributed to atebrin must be ascribed. [Names given to these conditions:—Climatic diarrhoea, Crete, Salonika or Cyrenaica disease, remind one of the Egyptian "tummy" so well known to our own men.] Rose is at some pains to emphasize that in the 10 years during which atebrin has been commonly used, no such symptoms have been attributed to it, and that even in large doses it has no fever-producing effect.

He reproduces a table of dosage and effects recorded by a number of workers (including British) on atebrin prophylaxis. *C. W.*

McMahon (J. C.). **A Brief Summary of the Results of Tests carried out on Certain Oils against Mosquito Larvae.**—*East African Med. Jl.* 1941. Nov. Vol. 18. No. 8. pp. 240–241.

The standard oil recommended for use in Kenya consists of 9 parts Shell diesel oil and 1 part Shell solar (gas) oil; under normal conditions this gives 100 per cent. kill of larvae in 90 minutes at a dosage of 12 gallons to the acre. The author has made tests of used motor engine oils and compares the results with those of the standard oil. The used motor oils have no toxic properties, and kill only by cutting off air supply; at twice the dose of the standard oil their results after 90 minutes were negligible; after 24 hours the results were very variable. Except in very heavy dosage, usually impracticable and uneconomical, these oils cannot be relied upon. The addition of kerosene must be heavy to produce reliable results; with less than 50 per cent. kerosene these mixtures are very slow in action. The addition of kerosene to used motor oil is therefore uneconomic.

C. W.

LEE (David B.). **Experimental Wells. Their Use in the Study of the Water Table in Relation to a Malaria Control Drainage Program.**—*Southern Med. Jl.* 1941. Aug. Vol. 34. No. 8. pp. 840–844.

An experimental well is a hole dug in the ground, 6 to 8 inches in diameter, lined with concrete subsoil pipes, the lower end of each pipe being notched to permit entry of ground water. The hole is dug deep enough so that it always contains water, even after drainage is instituted. A bench mark is set level with the top of the uppermost pipe. The study of the water table thus facilitated enables one to demonstrate the actual needs of malaria control drainage. In an area chosen for drainage in Pensacola, Florida, 25 such wells were constructed in appropriate localities ; daily readings were made for about one and a half years. The author describes how such observations enabled great economies to be made in carrying out a costly scheme. Two lessons learnt were : " Before and during drainage, study the water table by means of wells. Study the effects of a minimum drainage system before starting on any but obviously necessary fill." *N. W.*

MARTINS (Miguel L.). Considerações sobre a profilaxia da malaria. [**The Prevention of Malaria.**]—*Folha Med.* 1941. May 5. Vol. 22. No. 9. pp. 100–104.

MAIER (John) & COGGESHALL (L. T.). **Respiration of Malaria Plasmodia.**—*Jl. Infect. Dis.* 1941. July–Aug. Vol. 69. No. 1. pp. 87–96. With 15 charts.

Continuing the work of CHRISTOPHERS and FULTON [this *Bulletin*, 1938, Vol. 35, p. 709 ; 1940, Vol. 37, p. 190], the authors have devised a method of estimating the oxygen absorption of malarial parasites in the Warburg manometer in which centrifugation was eliminated. When the blood of the infected animal contained a sufficient number of parasites, enough was withdrawn to allow of 1 cc. for each Warburg flask, potassium oxalate (approximately 5 mgm. per 1 cc. of blood) being used as an anticoagulant. It is claimed that the method described has the advantage over that employed by the earlier observers, in that there is less risk of damage to the parasites during the manipulations. It was found that the oxygen uptake of normal blood was considerably less than that of infected blood, so much so that this could be ignored in estimating the quantity taken up by the parasites. It was also found that with increase in size of the parasites the oxygen absorbed increased. During the survival of the parasites glucose is used up and unless this is renewed the oxygen uptake declines. Mannose, fructose and glycerol can be employed by the parasites in place of glucose. In addition to *Plasmodium knowlesi*, which was most thoroughly investigated, four other species, viz., *P. inui* and *P. cynomolgi* of monkeys and *P. cathemerium* and *P. lophurae* of birds, were studied. *C. M. Wenyon.*

COGGESHALL (L. T.) & MAIER (John). **Determination of the Activity of Various Drugs against the Malaria Parasite.**—*Jl. Infect. Dis.* 1941. Sept.–Oct. Vol. 69. No. 2. pp. 108–113.

In a previous paper [above] the authors have described their technique for measuring the respiration of malarial parasites. In the

present paper it is shown how this technique can be applied to testing the influence of a drug on this respiration. From the results obtained with nine drugs it became evident that the effect of a drug on respiration could not be correlated uniformly with its therapeutic effect on experimental malarial infections. Qualitatively the activity of the drugs tested *in vitro* and *in vivo* could be correlated, with the exception of sulphadiazine and prontosil. The former had no action on the oxygen uptake of *P. knowlesi*, as was to be expected on account of its almost complete insolubility. When given to an infected monkey by stomach tube, however, it was just as effective as sulphanilamide, owing presumably to the production of a soluble derivative. The similar action of prontosil is due, no doubt, to its conversion into sulphanilamide. Quinine and atebrin inhibit respiration more effectively than sulphanilamide, which is more active therapeutically. Sodium sulphathiazole inhibits the respiration of *P. inui* and *P. cynomolgi* more than that of *P. knowlesi*. Therapeutically, however, the drug is most effective against *P. knowlesi*. This drug inhibited respiration of *P. cathemerium* but was quite without effect on infections in the canary. Sodium sulphathiazole affects equally the respiration of *P. knowlesi*, *P. inui*, *P. cynomolgi*, *P. cathemerium* and *P. lophurae*. Clinically it is very effective against *P. knowlesi*, only slightly so against *P. inui* and *P. cynomolgi* and quite without effect on *P. cathemerium* and *P. lophurae*. It seems clear, therefore, that though the effect of any drug on the respiration of a malarial parasite may be useful information, it cannot be relied upon to furnish an index of therapeutic efficiency. *C. M. W.*

HEGNER (Robert), WEST (Evaline) & DOBLER (Marian). **Further Studies of Hydroxyethylapocupreine against Bird Malaria.**—*Amer. Jl. Hyg.* 1941. Sept. Vol. 34. No. 2. Sect. C. pp. 132–139. With 3 figs.

In an earlier paper the authors and RAY [this *Bulletin*, 1942, Vol. 38, p. 124] showed that hydroxyethylapocupreine dihydrochloride was as effective as quinine hydrochloride in the treatment of certain bird malarial infections (*Plasmodium lophurae* in ducks, *P. relictum* in pigeons, *P. cathemerium* in canaries). In the present paper more precise details of the action of this drug are given. In the case of canaries infected with *P. cathemerium*, parasites disappeared more rapidly from the blood with larger doses than with smaller doses. The weight of treated birds remained constant, whereas that of untreated birds with developing infections rapidly declined. In ducks infected with *P. lophurae* quinine hydrochloride in daily doses of 0·05 mgm. per gm. of bodyweight was less effective in preventing increase in the number of parasites than hydroxyethylapocupreine in doses of 0·2 mgm. The latter drug administered to 9 ducks for four days before inoculation of parasites prevented the appearance of parasites in five, while in the remaining four only very scanty infections occurred which were no longer detectable after the sixth day. All of four controls died of their infections. As regards effectiveness it was shown that 0·2 mgm. daily were more effective than 0·1 mgm. daily. If these doses, or even larger ones of 0·4 mgm., were administered on alternate days instead of daily the infections were hardly influenced. They progressed as in untreated birds till death took place. Both quinine and hydroxyethylapocupreine in ducks infected with *P. lophurae* and in canaries infected

with *P. cathemerium* brought about a reduction in the number of merozoites produced by the schizonts. A number of other drugs, mostly sulphanilamide derivatives, were tested but none had any marked effect on the infections. *C. M. W.*

KIKUTH (W.) & MUDROW (L.). Ueber die Entwicklung der Sporozoiten der Malariaparasiten. [**Development of Sporozoites of Malarial Parasites.**]—*Zent. f. Bakt.* I. Abt. Orig. 1941. July 7. Vol. 147. No. 4. pp. 284–288.

The authors refer to two papers by MISSIROLI describing the development of sporozoites of bird malarial parasites when injected into birds [this *Bulletin*, 1940, Vol. 37, p. 671; 1942, Vol. 39, p. 123]. They point out that the second paper is mostly a reproduction of the first and fails to give any new information, though it criticizes the results of similar observations made by the authors [this *Bulletin*, 1940, Vol. 37, p. 671]. According to Missiroli the sporozoites in the salivary glands of mosquitoes may be mature or immature. In the former case the nucleus contains four chromatin granules, a preparation for the development which is supposed to take place immediately the sporozoites are injected into the bird. This development, completed in 24 hours, consists of the formation extracellularly in lymph spaces of four nuclear schizonts which divide into merozoites. These merozoites may enter red blood corpuscles to grow into pigmented erythrocytic schizonts or be taken up by reticulo-endothelial cells within which they develop into exoerythrocytic schizonts. The authors cannot accept this cycle of development. They assert that all sporozoites in salivary glands are mature and that the varying nuclear appearances are the result of the drying technique. They hold that in the bird there is no immediate development but that this commences only after a delay period of several hours. Before this the uninucleate sporozoite becomes a uninucleate rounded body which can be seen after 16 hours within cells of the reticulo-endothelial system, either at the site of inoculation or in the internal organs. Nuclear multiplication takes place and in two or three days' time the now multinucleate schizonts divide into merozoites. These, if they fail to enter other reticulo-endothelial cells, find their way into red blood corpuscles. Thus the authors hold that Missiroli is wrong in maintaining that sporozoites in the salivary glands vary in their maturity, that their first development in the bird is extracellular and that four-nucleated schizonts giving rise to four merozoites are produced. *C. M. W.*

BELTRAN (Enrique) & LARENAS (Raúl). Producción de malaria aviar con *Plasmodium gallinaceum* por vía oral. [**Production of Avian Malaria with *P. gallinaceum* by the Oral Route.**]—*Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1941. June. Vol. 2. No. 1. pp. 87–94. English summary (5 lines).

The authors have confirmed the observation of SHORTT and MENON [this *Bulletin*, 1941, Vol. 38, p. 338] that chickens may be infected with *Plasmodium gallinaceum* by the introduction of infected blood into the mouth. In the present instance the authors introduced into the mouths of 34 two-weeks-old chicks infected citrated blood, care being taken to avoid any damage to the buccal mucosa. In four of the chicks infection resulted. *C. M. W.*

Young (Martin D.). **The Oral Transmission of *Plasmodium relictum* in the Pigeon.**—*Public Health Rep.* 1941. July 11. Vol. 56. No. 28. pp. 1439–1440.

Shortt and Menon have recently reported the oral transmission of *P. knowlesi* and *P. gallinaceum*. The present author has confirmed this work by infecting pigeons with *P. relictum* by the oral route, using blood obtained from infected birds by heart puncture. So far 10 pigeons have been given blood into the crop through a catheter attached to a syringe, and of these seven became infected. "The malaria has been transferred through two consecutive passages by oral administration." "This adds further evidence to that recently obtained on the exo-erythrocytic forms of malaria, indicating that these parasites may be able to live in types of tissue other than blood." *C. W.*

Beltran (Enrique). Estado actual de nuestros conocimientos acerca del *Plasmodium gallinaceum* Brumpt, 1935. [**The Present State of Knowledge of *P. gallinaceum*.**]—*Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1941. June. Vol. 2. No. 1. pp. 95–113. [58 refs.] English summary.

Versiani (Valdemar) & Gomes (Brenno Furtado). Sobre um novo hematozoário da Galinha—"Plasmodium juxtanucleare" n. sp. (Nota prévia.) [**A New Hematozoon of the Fowl, *Plasmodium juxtanucleare* n. sp.**]—*Rev. Brasileira Biol.* Rio de Janeiro. 1941. June. Vol. 1. No. 2. pp. 231–233. English summary (4 lines).

The authors announce their discovery in two domestic fowls in the State of Minas Geraes, Brazil, of a small malarial parasite resembling *P. vaughani*, *P. rouxi* and *P. nucleophilum*. The parasite has a tendency to be in contact with the nucleus of the host cell and is accordingly given the name *P. juxtanucleare*. It is readily inoculable to chickens, while one of two turkeys inoculated became infected. A number of other birds, including pigeons and canaries, appear to be refractory. A fuller description of the parasite is promised in a further paper. *C. M. W.*

Coggeshall (L. T.). **Infection of *Anopheles quadrimaculatus* with *Plasmodium cynomolgi*, a Monkey Malaria Parasite, and with *Plasmodium lophurae*, an Avian Malaria Parasite.**—*Amer. Jl. Trop. Med.* 1941. July. Vol. 21. No. 4. pp. 525–530. With 1 fig.

The monkey malarial parasite, *Plasmodium cynomolgi*, used in these experiments was discovered in a *Macacus cynomolgus* which had been acquired from an animal dealer in the United States. The monkey, which had come from Java, was not suspected of having a malarial infection. It was accordingly inoculated with *P. knowlesi*. When the malarial infection developed, this was found to be a mixed one of *P. knowlesi* and *P. cynomolgi*. The administration orally of three 1·0 gram doses of sulphanilamide eradicated the *P. knowlesi* infection, leaving the *P. cynomolgi*, which was sub-inoculated into rhesus monkeys. In a previous experiment a pure infection of *P. inui* had been obtained in a similar manner from a mixed infection with *P. knowlesi*. In rhesus

monkeys *P. cynomolgi*, which closely resembles *P. vivax*, produces a moderately severe infection followed by recovery from the acute attack. Parasites, however, remain in the blood for many months.

It was found that *Anopheles quadrimaculatus*, the principal vector of human malaria in the United States, may readily become infected when fed on monkeys harbouring *P. cynomolgi*. In a total of 250 mosquitoes dissected 30 per cent. were infected. In some lots as many as 80 per cent. of the mosquitoes were infected. The infections were in many cases heavy, over 1,000 oöcysts being counted on a single stomach. Sporozoites appear in the salivary glands on about the fifteenth day. Such infected mosquitoes transmitted the infection to normal rhesus monkeys but failed to do so to general paralytics. Attempts were made to infect *A. quadrimaculatus*, *A. punctipennis* and *Culex pipiens* with *P. knowlesi* by feeding on infected monkeys and on general paralytics, but without any success. The mosquito *A. quadrimaculatus* was also infected with *Plasmodium lophurae*, a parasite which had originally been isolated from a Borneo fire-backed pheasant by inoculation into chickens. The mosquitoes fed on infected chicks became infected to the extent of 46 per cent. The infections were, however, not heavy, a maximim of 60 oöcysts being counted on one stomach. In this case salivary gland infections have not been observed. Development of this parasite in *Culex pipiens* and *Aëdes aegypti* was also observed. Though *A. quadrimaculatus* was so heavily infected with *P. cynomolgi*, attempts to infect it with *P. inui* were not successful. *C. M. W.*

TROPICAL OPHTHALMOLOGY.

A Review of Recent Articles.—XXXIX.*

Conjunctiva.—Bidyadhar[1] has reported from Sonpur State in India the occurrence of two cases of an *acute follicular conjunctivitis* which were of the type described by Béal. The onset of the inflammation was sudden, with oedema of the lids (most marked in the lower lids), and intense vascular engorgement in the fornices accompanied by the development of follicles. The pre-auricular glands were enlarged but free from tenderness. The condition cleared up in a little more than two weeks under simple treatment. Inclusion bodies were absent and cultures from the conjunctiva proved negative. Moderate eosinophilia and lymphocytosis were present. Both patients had suffered from previous attacks of conjunctival inflammation.

Trachoma.—McKelvie and Kirk[2] have recorded their experience of the use of sulphonamides in the treatment of trachoma in the Sudan.

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* For the 38th of this series see Vol. 38, pp. 723–724.

[1] Bidyadhar (Nabin Kishore). Acute Follicular Conjunctivitis resembling Béal's Type. Report of Two Cases, with a Short Review of the Literature. —*Arch. Ophthalm.* 1941. Oct. Vol. 26. No. 4. pp. 587–594. [30 refs.]

[2] McKelvie (A. R.), Kirk (R.) & Holder (H. J.). Observations on the Chemotherapy of Trachoma.—*Amer. Jl. Ophthalm.* 1941. Sept. Vol. 24. No. 9. pp. 1035–1043. [45 refs.]

The preparations used were sulphanilamide (Prontosil album), proseptasine (M. & B. 120), and sulphapyridine (M. & B. 693); no difference in the therapeutic effect of these drugs was noticed. The authors state that trachoma without any subjective symptoms (which they term "subclinical trachoma") exists amongst the Sudanese; this form is only potentially important in that it lowers resistance to secondary infection and it is unaffected by sulphanilamide therapy. Severe forms of the disease, however, complicated by pannus and keratitis, respond in a satisfactory manner both subjectively and objectively, though inclusion bodies may not necessarily disappear. It is suggested that perhaps pannus, keratitis and other serious clinical manifestations may be the result of secondary infection and that trachoma itself may be a non-pathogenic, or only mildly pathogenic, infection of no clinical importance. Secondary infections in 200 patients were due to the gonococcus in 18·5 per cent., to the Koch-Weeks bacillus in 65·5 per cent., to the pneumococcus in 2 per cent., and to the Morax-Axenfeld bacillus in 14 per cent.

In Shanghai, Lee, Rottenstein and Chao[3] have found that sulphanilamide, when administered orally, affords a rapid relief from the acute subjective symptoms of trachoma. Their experience of the local application of the drug, however, has not been so favourable. They attribute this to the fact that, as proved by their experimental studies on the human subject, the concentration of the drug in the aqueous induced by the local application, though high, is only short-lived, whereas that induced by oral administration, though considerably lower, is of much longer duration. They consider that a concentration of 3 mgm. per 100 cc. of aqueous, if persistent, is more beneficial than a much higher concentration of short duration.

Robson and Scott[4] have studied the action of albucid soluble in the treatment of corneal ulcer, induced in the rabbit by the local inoculation of *Ps. pyocyanea*. The drug was found to be markedly effective in controlling the infection provided it was used within one hour after the inoculation, but it became progressively less effective if its application was delayed. After a delay of 12 hours the beneficial effect was still apparent though only slight. Concentration of the drug up to 30 per cent. has been used in clinical work without causing signs of irritation or other ill effects. Albucid is highly soluble and is stated to penetrate the cornea readily. It is the sodium salt of sulphacetamide.

Gonorrhoeal Ophthalmia.—Lee and Lum[5] have found that in the treatment of gonococcal ophthalmia the combined use of a sulphanilamide and milk injections is more efficacious than either drug treatment or injection treatment employed alone. The authors' observations were made on seventeen children from four to nine years of age who had been infected in an institution. The inflammation had been present for about ten days before admission and the preparation used was sulphanilyldimethylsulphanilamide.

[3] Lee (Otis S.), Jr., Rottenstein (Hans S.) & Chao (Ho Yung). Local Treatment of Trachoma with Sulfanilamide with Special Reference to its Concentration in the Aqueous Humor.—*Chinese Med. Jl.* 1941. Sept. Vol. 60. No. 3. pp. 207–221. [15 refs.]

[4] Robson (J. M.) & Scott (G. I.). Local Effectiveness of Sodium Sulphacetamide (Albucid Soluble) in Treatment of Experimental Ulcers of the Cornea.—*Brit. Med. Jl.* 1942. Jan. 3. pp. 5–8. With 2 figs. [16 refs.]

[5] Lee (Otis S.), Jr. & Lum (Francis K.). Gonorrheal Ophthalmia. Treatment with a Sulfanilamide Derivative and Injections of Milk.—*Arch. Ophthalm.* 1941. Aug. Vol. 26. No. 2. pp. 268–275.

Onchocerciasis.—A review of ocular onchocerciasis has been made by QUEVEDO[6]. He states that the ocular troubles are caused by the presence of microfilariae in the tissues of the eye and are not due to a toxin produced by the adult parasite; he has never failed to find microfilariae in any eye lesion caused by onchocerciasis. Eye symptoms appear fairly soon after the formation of a fibrotic nodule under the skin—irritation, vascular congestion, lachrymation and photophobia. Later the disease tends to assume three types—(1) a subacute inflammation of the anterior segment of the eyeball, (2) a milder reaction affecting the posterior segment—choroid, retina and optic nerve, and (3) a combination of these two types. The keratitis is characteristic; small whitish opacities appear near the limbus at each extremity of the horizontal meridian of the cornea. These are due to the inflammatory reaction excited by the presence of the bodies of dead microfilariae. Frequently a fine deposit of brown pigment may be observed in the affected area. Vascularization is a later change. Microfilariae can be seen free in the anterior chamber and a subacute plastic iritis is common. The pupil is often elongated in the vertical meridian. A chronic form of chorio-retinitis usually occurs in the late stages of the disease and sometimes a condition resembling retinitis pigmentosa may develop. Fibrotic nodules which contain the adult parasites must be searched for and excised when found.

Deficiency Disease.—The ocular condition of 34 patients suffering from vitamin deficiency diseases has been investigated by RAMAN[7] and he states that he found evidence of a lesion of the optic nerves in twenty. The degree of nerve involvement varied from a slight concentric contraction of the visual field in five cases and a marked contraction in thirteen to a primary optic atrophy in two. Pallor of the temporal side of the optic disc was present in two patients. Twenty-one of the patients suffered from a disease of the beriberi type, ten from pellagra and one patient suffered from both beriberi and pellagra. Two cases of diabetes mellitus are included in the series.

MÉTIVIER[8] has noted in Trinidad an epithelial dystrophy of the cornea which he believes is due to a lack of vitamin B_2. He calls the condition "essential corneal epithelial dystrophy" and describes it as "a condition in which a geometrical arrangement in a double line, running transversely across the cornea, at the level of the lower part of the pupillary area, shows a faint greyish-white disturbance of the epithelium which is made up of fine points like dots and commas." The affected area stains well with fluorescine. There is a complete absence of conjunctival or ciliary injection. Nursing mothers are specially liable to the trouble. Patients complain of photophobia and a mistiness of vision during the day. A complaint of defective vision indicates an added nutritional amblyopia. This latter condition

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[6] QUEVEDO (Arturo). Ocular Onchocerciasis.—*Amer. Jl. Ophthalm.* 1941. Oct. Vol. 24. No. 10. pp. 1185–1189.

[7] RAMAN (T. K.) & ABBU (C.). Lesions of the Optic Nerve in Vitamin B_1 Deficiency.—*Jl. Indian Med. Assoc.* 1941. July. Vol. 10. No. 10. pp. 417–422. With 7 figs.

[8] MÉTIVIER (V. M.). Eye Disease due to Vitamin Deficiency in Trinidad. Tropical Nutritional Amblyopia; Essential Corneal Epithelial Dystrophy; Conjunctional Bleeding in the Newborn.—*Amer. Jl. Ophthalm.* 1941. Nov. Vol. 24. No. 11. pp. 1265–1280. With 3 figs. [45 refs.]

is stated to be also due to a deficiency of vitamin B_2 and is characterized by a partial atrophy of the optic nerve which leads to a pallor of the temporal portion of the papilla. The area involved may vary from a little less than half up to three-quarters of the disc. The author remarks that vitamin A deficiency is unimportant in Trinidad and that keratomalacia is rare. Beriberi and pellagra are clinical curiosities there.

JOHNSON[9], in a paper on the ocular effects of vitamin-B-complex deficiency, states that in the University Hospitals of Cleveland, Ohio, the routine treatment of keratitis rosacea is a daily intravenous injection of 1 or 2 mgm. of riboflavin and the oral administration of three teaspoonsful of elixir of vitamin B complex until the lesion shows signs of healing. Two injections usually suffice to cure mild cases, but treatment may be required for a week in severe attacks, especially if there is a complete absence of HCl. He suggests that a deficiency of riboflavin must seriously impair oxidization in the cells of the cornea, since, in such an avascular structure, the process is dependent upon the presence of Warburg's yellow enzyme. Proliferation of capillaries from the limbus would seem to be an attempt to relieve localized anoxaemia by bringing haemin substances to the spot.

The triennial report of the Madras Government Ophthalmic Hospital for the years 1938–1940 omits clinical remarks but records statistics which are valuable to those interested in the incidence of eye disease in the tropics.

The hospital has now reached a considerable size and contains beds for 170 in-patients. A slight fall occurred in the number of out-patients during the triennium—from 39,953 in 1938 to 35,868 in 1940; a rise, however, occurred in the number of in-patients in the same period from 5,108 to 5,842. Macular keratitis appears to have greatly declined and only 38 cases of the disease were treated in 1940. Trachoma accounted for 1,708 admissions in 1940, Koch-Weeks catarrh for 2,216, other forms of acute infection of the conjunctiva for 1,206, and diplo-bacillary inflammation for 1,355; 466 patients were admitted for keratomalacia and 621 for keratomalacia with xerosis of the conjunctiva during the triennium. Retinitis pigmentosa accounted for 234 out-patient admissions during the period, injury to the macula by the sun for 150, and ametropia for 15,154; astigmatism was the most common error of refraction. There were 682 cases of glaucoma and 3,036 of cataract treated as in-patients during 1940 and 9,517 operations were performed during that year, 2,377 being for cataract. The combined operation with capsulotomy for cataract, and sclero-corneal trephining for glaucoma, appear to have been the operations of choice for these conditions. In addition to the above, 618 operations were performed by the Honorary Medical Staff of the hospital.

H. Kirkpatrick.

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[9] JOHNSON (L. V.). Clinical Ocular Conditions associated with Vitamin B Complex Deficiency.—*Amer. Jl. Ophthalm.* 1941. Nov. Vol. 24. No. 11. pp. 1233–1240. With 8 figs. (2 coloured on 1 plate.)

VENOMS AND ANTIVENENES.

ROSENFELD (Samuel) & RUBINSTEIN (Joshua). **Separation of the Coagulant from the Toxic Principles of the Venom of the Australian Tiger Snake** (*Notechis scutatus*). **With Remarks on the Mode of Action of the Coagulant.**—*Jl. Lab. & Clin. Med.* 1941. Oct. Vol. 27. No. 1. pp. 45–49. With 1 fig. [10 refs.]

The venom of *N. scutatus* is one of the most powerful snake poisons known and is toxic by virtue of the neurotoxin it contains, but it also contains a powerful coagulant substance comparable with that of the S. American vipers *Bothrops jararaca* and *B. atrox*, and of the Australian black snake *Pseudechis porphyriaceus*. This coagulant property has been used to arrest severe capillary haemorrhage by local application. The authors have found that the addition of 5 per cent. HCl to an equal volume of 1 in 1,000 solution of the venom in physiological saline leads to the formation of a precipitate which contains the whole of the coagulant principle, leaving the toxin in solution. The precipitate is soluble in distilled water, and three precipitations are necessary for complete separation.

The coagulant factor is harmless on injection into mice, even in an amount equivalent to that contained in 3,000 minimal lethal doses of the original venom ; the toxic factor has no coagulating action. The coagulant factor behaves like thrombokinase plus calcium, readily converting prothrombin to thrombin. *C. W.*

GHOSH (B. N.), DE (S. S.) & CHAUDHURI (D. K.). **Separation of the Neurotoxin from the Crude Cobra Venom and Study of the Action of a Number of Reducing Agents on it.**—*Indian Jl. Med. Res.* 1941. Apr. Vol. 29. No. 2. pp. 367–373.

" 1. A very active sample of neurotoxin has been separated from the crude cobra (*Naja tripudians*) venom by fractional precipitation of impurities with sodium sulphite, adsorption of the neurotoxin on tungstic acid, followed by its elution and further fractional precipitation from the eluted solution by treatment with ammonium sulphate. The pigeon and mouse units of this neurotoxin were 0·0061 mg. and 0·022γ respectively.

" 2. The action of a number of reducing agents on solutions of cobra neurotoxin has been tried *in vitro* and it has been found that sodium bisulphite, zinc and hydrochloric acid (N/10) ascorbic acid and cysteine can destroy the neurotoxin to a marked extent."

ARANTES (J. B.) & NEIVA (Cicero). I. Toxicidade do veneno crotálico para o cobaio. a. Via subcutanea. b. Via intra-muscular. [**Toxicity of the Venom of** *Crotalus terrificus* **by the Subcutaneous and Intramuscular Routes.**]—*Brasil-Medico.* 1941. July 5 & 12. Vol. 55. Nos. 27 & 28. pp. 465–466 ; 477–478. English summaries (7 lines).

The authors have found by experiment that the minimum lethal doses, for guineapigs weighing 330 to 380 gm. are—subcutaneously 0·025 mgm., intramuscularly 0·013 mgm. *C. W.*

Neiva (Cicero) & Arantes (J. B.). III. Anagotoxia para o veneno crotálico em águas da prata. [**Antagonism of Prata Mineral Water to the Venom of** *C. terrificus.*]—*Brasil-Medico.* 1941. Aug. 30. Vol. 55. No. 35. pp. 598–599.

" In experiments on guinea pigs weighing 330 to 380 gm. the minimum lethal dose of the rattlesnake poison was ascertained by intramuscular injections of 0·013 mgr. and subcutaneous injections of 0·025 mgr. A measured quantity of mineral water was added to the doses of poison to make a solution that was injected into guinea pigs. The experiments carried out show that when mineral water and poison of *Crotalus terrificus* are brought together there is an antagonistic effect of the water to the poisonous substance. It signifies a counteraction of mineral water to venom in which the former may almost exactly neutralize or weaken the action of the latter.

" This paper deals with the antitoxic effect of Prata mineral water on venom of *C. terrificus* in laboratory experiments and duplication of these researches near the mineral water springs. The action of the Prata bottled mineral water neutralizes 0·018 mgr. of crotalic poison when injected intramuscularly. In the locale of the springs superior results were obtained by the same methods. [See also this *Bulletin*, 1941, Vol. 38, p. 662.]

Neiva (Cicero) & Arantes (J. B.). IV. Anagotoxia para o veneno crotálico em águas de Caxambú. [**Antagonism between Caxambú Waters and Crotaline Venom.**]—*Brasil-Medico.* 1941. Sept. 6. Vol. 55. No. 36. pp. 609–610. English summary.

" Experiments on guinea pigs of the antitoxicity of Caxambú mineral water to *Crotalus terrificus* poison employing subcutaneous and intramuscular injections are described. Formerly the minimum lethal dose to guinea pigs weighing 330 to 380 gm. was ascertained. When injected by intramuscular route it was found that water rich in magnesium salts revealed greater antitoxicty than that of alkaline water. Subcutaneously the former type was negative in action but the latter produced the inactivation of the poison studied."

Neiva (Cicero) & Arantes (J. B.). V. Anagotoxia para o veneno crotálico em águas de São Lourenço. [**Antagonism between São Lourenço Waters and Crotaline Venom.**]—*Brasil-Medico.* 1941. Sept. 13. Vol. 55. No. 37. pp. 632–633. English summary.

" Guinea pigs were protected against rattlesnake poison by injections of mineral water from S. Lourenço. The experiments were carried out in such a way that there was no loss among the guinea pigs which were injected with varying amounts of crotalic poison plus mineral water. There is an antagonistic action between mineral waters and rattlesnake poison so that if guinea pigs are injected subcutaneously with a dilution of an m.l.d. of venom of *Crotalus terrificus* in S. Lourenço waters no death is observed. These results conform with others observed in similar experiments in which the venom-mineral water solution was introduced intramuscularly."

Subedar (S. A.). **Snake Venom in Therapeutics.**—*Med. Digest.* 1941. Oct. Vol. 9. No. 10. pp. 282–287.

A general account in which reference is made to the use of cobra venom in epilepsy and cancer, and of viper venom as a haemostatic.
C. W.

Pasricha (C. L.) & Abedin (Z.). **The Sterility of Snake Venom Solutions.**—*Indian Med. Gaz.* 1941. May. Vol. 76. No. 5. pp. 276–277.

The authors examined 25 snake venom solutions, used for haemostatic or analgesic purposes, for the presence of aerobic and anaerobic bacteria. Of 11 cobra venoms 2, and of 14 viper venoms 6, were contaminated. The reason for the examinations was the occurrence of a severe reaction after subcutaneous injection of one of the solutions.

Crude venom is grossly contaminated when collected; the most satisfactory method of sterilization is filtration through an asbestos filter.
C. W.

Githens (Thomas S.). **The Polyvalency of Crotalidic Antivenins. IV. Antinecrotic, Anticoagulant and Antiproteolytic Actions.**—*Jl. Immunology.* 1941. Oct. Vol. 42. No. 2. pp. 149–159. With 1 plate.

Death from snake venom is commonly due to the action of neurotoxin, and antivenenes are standardized by their ability to neutralize these, but little or no attention appears to have been given to the antigenic relationship of the other constituents of the venoms. The author has therefore studied the local necrotic factor, the blood-clotting factor and the proteolytic factor, determining quantitatively their effective doses and the ability of antivenenes to neutralize them. In this study the venoms of 26 species of pit vipers, two of true vipers and one of an elapine snake were used, and three antivenenes, polyvalent Crotalidic, Cascabel (monovalent against *C. d. durissus*) and Bothropic (monovalent against *B. atrox*).

The content of necrotic factor of the pit vipers is more constant than that of the neurotoxin, and nearctic Crotalidic and Cascabel antivenenes are equally able to neutralize the necrotic factors of various venoms. The content of the blood-clotting factor of different lots of venoms varies very widely, even within the same species, and bears no relation to the other factors. Antivenenes are able to neutralize the clotting factor, but are less effective than against the neurotoxic and necrotic factors. Different lots of venom of the same species agree in their proteolytic activity, but the various species of pit vipers show great differences. Antivenenes are irregular and uncertain in their neutralizing action and show no evidence of specificity.

Full protocols are given of the experiments on which these conclusions are based.
C. W.

Grasset (E.). **On the Standardisation of African Viper ("Bitis arietans") and Cape Cobra ("Naia flava") Antivenenes.**—*Bull. Health Organisation.* (League of Nations.) 1940/41. Vol. 9. No. 4. pp. 476–491. With 4 graphs.

"The following conclusions can be deduced from the experiments undertaken with a view to determining whether the method of Banic

and Ljubetic as modified by Ipsen and proposed by the Permanent Commission on Biological Standardisation for the assay of European viper antiserum could be applied to the standardisation of African viper and Cape cobra antivenenes :

" 1. By means of this method of assay at various levels, it is possible to titrate with satisfactory accuracy the neutralising power of the monovalent African viper (*Bitis arietans*) antiserum and to assess the amount of *Bitis* antibody contained in the polyvalent viper-cobra antivenene.

" 2. The method can also be applied with satisfactory accuracy to the titration of the monovalent *Naia flava* antiserum and of the amount of Naia antibody contained in the polyvalent viper-cobra antivenene.

" 3. Thus it is possible, by means of this method, to assess the amount of African viper and Cape cobra antibodies contained in the polyvalent antivenene prepared by the South African Institute for Medical Research."

Bokma (H.). Nog eens een beet van een zeeslang. [**Bite by a Sea Snake.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1942. Jan. 13. Vol. 82. No. 2. p. 87.

The patient, a strongly built Javanese male, stated that at 6 a.m. on October 6th, 1941, when he was fishing in shallow water he kicked a snake which bit him on the left foot. When seen two hours later he complained of a " feeling of paralysis " over his whole body. On the dorsum of the left foot, over the outer metatarsals was a wound, 1 cm. in length. No other symptoms were present ; reflexes were normal, pupils reacted to light and convergence ; urine not obtainable. He was given 100 cc. of antivenene intravenously. The next day he passed 400 cc. of urine, coffee-coloured. He complained now of stiffness of the legs, and he could sit only with difficulty, and the legs were spastic on passive movement ; knee-jerks and Achilles' reflex not elicited. Cremasteric and abdominal reflexes present ; no pain on passive movement. Urine was light brown, amphoteric in reaction, sp. gr. 1023, marked reaction for albumen, no biliary pigments or erythrocytes. General condition good. Next day, legs less spastic, reflexes present, albuminuria less, was able to walk, but leg movements were still stiff. Twenty-four hours later (October 9th) he was well, urine clear and free from albumen. At no time was there any swelling of the parotids or sweating, nor was there any circulatory or respiratory disturbance.

H. H. S.

Bokma (H.). Doodelijke vergiftiging door den beet van een zeeslang. *Enhydrina schistosa* (Daudin). [**Fatal Poisoning from the Bite of the Sea Snake** *E. schistosa.*]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1941. Sept. 9. Vol. 81. No. 36. pp. 1926–1931. English summary.

" Description of a case of sea-snake poisoning (Enhydrina schistosa (Daudin)). The symptoms were : marked muscular paralysis, accentuated swelling of the parotis gland, pain and difficulty in swallowing, difficulty of speech, hemoglobinuria (there was no hemolysis). Hyperhydrosis.

" The patient died 24 hours after the snake-bite, the pulse becoming thread-like, the respiration becoming slower and weaker.

" *Post mortem.* Hyperemia of the lungs and enormous ectasia of the stomach and the intestines.

" Microscopically. Necrotic skin lesion, surrounded by inflammation at the site of the bite. Hyperemia of the internal organs."

DE MAGALHÃES (Octavio) & GUIMARÃES (Rubens). Algumas observações sobre acidentes pela picada dos escorpiões (*T. serrulatus*). [**Observations on the Results of the Sting of the Scorpion** *Tityus serrulatus.*]—*Brasil-Medico.* 1941. July 5. Vol. 55. No. 27. pp. 461–465. With 3 figs.

Three cases are reported. The first is of a young man stung at the age of five. The history given is of immediate and persistent vomiting, first of food, later of bile and blood, with dyspnoea and, in a few hours, paresis of the right arm and leg. No serum was available for treatment. At the time of examination, 17 years later, the right arm was wasted, the hand in a position of extension and of *main en griffe.* The right hip and knee joints were somewhat flexed, the foot being rotated outwardly. There was spasticity of the muscles of the right arm and contracture of the tendo Achillis, with positive Babinski, clonus and exaggerated tendon reflexes. The left side was normal. [The period between the infliction of the sting and the examination by the authors was long ; but the authors appear to be in no doubt that the paresis was due to the sting.]

The second case was that of a child stung on the left foot. Vomiting, dyspnoea, midriasis, bradycardia, suffusion of the conjunctivae and excessive bronchial secretion followed. Anti-scorpion serum was given, 5 cc. into the cisterna magna and 30 cc. intravenously ; this was followed by urticaria and sweating, treated with adrenalin. More serum was given and the child's condition improved, but at the site of the sting there was intense oedema with formation of an abscess which burst spontaneously. The third patient, a man of 23, was bitten on the hand and treated with serum ; the general condition remained good but the whole hand was swollen. The patient recovered.

C. W.

HARGREAVES (W. H.) & MACKENZIE (K. G. F.). **Spider Bite simulating Acute Abdomen.**—*Jl. Roy. Army Med. Corps.* 1942. Jan. Vol. 78. No. 1. pp. 37–39. With 1 fig.

A Polish soldier in Palestine was brought to hospital with what was thought to be an acute abdominal condition, diagnosed tentatively as acute appendicitis. He was slightly cyanosed, shocked, with shivering, profuse sweating, temperature 97°F., pulse 88 and weak, and complaining of intense pain in the abdomen. He had vomited on the way to hospital and the abdomen was rigid, tense and board-like, and very tender. Another diagnosis suggested was perforated peptic ulcer. The patient had been quite well till two hours before admission when he felt a sharp pain in the right gluteal region, where he was bitten by a spider, which proved to be a female *Latrodectus lugubris.* The pain, like cramp, spread over the whole body within a minute and vomiting soon followed.

He was given morphia and, intravenously, 10 cc. of 10 per cent. calcium gluconate. He was very ill for three days and the abdominal pain and tenderness persisted. Blood concentration was marked :

red corpuscles 8,920,000 per cmm., haemoglobin 120, but white cells 10,400 and differential count normal. Two species of Latrodectus are found in Palestine, the black *L. lugubris* and the black with red spots, *L. tredecimguttatus*. The venom is said to be a toxalbumen some 15 times as potent as that of the prairie rattlesnake, *Crotalus albicans*.

[The results of bites by *L. mactans* and other species have been repeatedly described in this *Bulletin*, see 1935, Vol. 32, pp. 673, 914, 915 ; 1936, Vol. 33, pp. 401, 402, where an account is given of symptoms like those above, following an experimentally inflicted bite ; 1939 Vol. 36, pp. 570, 571, 867, 868 ; 1940, Vol. 37, pp. 516, 517.]

H. H. S.

MISCELLANEOUS.

Dyer (Brian R.). **Studies of Ground Water Pollution in an Alkaline Alluvium Soil.**—*Indian Jl. Med. Res.* 1941. Oct. Vol. 29. No. 4. pp. 867–889. With 5 figs. & 1 plate. [Summary appears also in *Bulletin of Hygiene*.]

During the past ten years many bored latrines have been installed in the East. There is a possibility that contamination of shallow wells may occur when the latrine extends down into the soil water. An investigation was carried out by the Punjab Public Health Department to determine to what extent is the spread of pollution introduced into subsoil water.

A bore hole was sunk to sub-soil water level in an area free from any known source of pollution. At measured distances from this bore-hole hand pumps were introduced tapping the sub-soil water. After carrying out bacteriological, chemical and physical tests to assess the normal quality of the sub-soil water, night-soil from a small community of persons was introduced into the borehole daily.

The findings reported in the paper apply only to the upper soil or *crust*, which has a high alkalinity and contains a high percentage of sodium sulphate.

Pollution as determined by the " Eijkman method " (positive being acid and gas in MacConkey broth incubated at 45°C. in sample of 50 ml. or less) passed the 5-foot zone but did not reach the 10-foot zone.

Pollution as shown by the " MacConkey method " (positive being acid and gas in MacConkey broth incubated at 37°C. in sample of 50 ml. or less) passed the 15-foot zone but did not reach the 20-foot zone.

Cl. welchii was not encountered at any time during the experiment. (40 ml. of water tested by method of Wilson and Blair).

At no time was there any variation in *p*H which could be related to pollution. There was no odour nor foaming of samples from hand-pumps. Dissolved oxygen determinations correlated well with the bacteriological findings.

The author gives a detailed description of the layout of the experiment with a diary of procedure, and the results are illustrated in graphical and tabular form. *E. Windle Taylor.*

Stransky (Eugene) & Pecache (Leon V.). **Noma in the Philippines.** —*Jl. Philippine Med. Assoc.* 1941. Oct. Vol. 21. No. 10. pp. 501–507. [11 refs.]

Noma is not rare in the Philippines, and the authors present records of 42 cases. The usual actiological factors are stated to be ileocolitis, measles and tuberculosis; none was due to malaria, but one was associated with acute lymphatic leucaemia. Two of the patients were aged 6, one aged 9 and two aged over 50, the remainder were under 5 years. Of the 42, five recovered, 14 died in hospital and 23 were taken home against advice and probably died. The post-mortem findings of the 14 are given; septico-pyaemic conditions were found in seven, ileocolitis in seven, bronchopneumonia in five, and tuberculous foci in three. The septico-pyaemic processes are, like noma itself, secondary conditions due to lack of resistance of the body brought about by ileocolitis, measles and other infections. There were three cases of manifest vitamin A deficiency.

The patients are febrile if the causative condition is a febrile disease, and the blood picture retains the characters of the predisposing illness; there is a remarkable lack of pain. Treatment depends on the aetiology; in septico-pyaemic conditions sulphonamides may be of use. Prophylaxis is more important and in this improvement in the standard of nutrition and the further development of child welfare play their part.

C. W.

Tratman (E. K.). **A Note on the Treatment of Cancrum Oris.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1941. June. Vol. 5. No. 1. pp. 31–33. With 3 figs.

The author has treated 11 cases by the method now advocated, with six cures, but two of the patients died before the treatment had time to make an impression. General treatment entails the administration of one of the sulphonamide preparations, by the mouth or, preferably, by injection, in maximum doses continued for several days, but it is essential that a blood examination should first be carried out to exclude agranulocytosis, which may simulate some of the symptoms of cancrum oris. The author has used soluseptasine chiefly. Local treatment consists of swabbing with eusol and wiping away the sloughs, and the immediate application of a fresh 5 per cent. solution of gentian violet. It is important to make sure that this solution actually comes into contact with the tissues, and is not held off by a layer of saliva or mucin. The gentian violet should be held in contact for not less than 30 seconds, and this local treatment is repeated every four hours except during sleep. Teeth and bone sequestra should only be removed when thoroughly loose. The patients should be given a liberal diet with plenty of vitamin C; isolation of the patient should be practised and gloves and masks should be worn by the attendants.

C. W.

McMillen (Sim I.). **Successful Treatment of Noma with Solution of Formaldehyde. Report of Six Additional Cases.**—*Amer. Jl. Dis. Children.* 1941. Sept. Vol. 62. No. 3. pp. 590–595. With 1 fig.

Records are given of six consecutive cases in native children in Sierra Leone; all were treated with formaldehyde (B.P.) and all

recovered, whereas earlier experience with other methods of treatment had indicated a case mortality rate of about 90 per cent. The method is as follows:—no attempt is made to excise all infected tissue, but hanging shreds and loose teeth may be removed; the ulcer is carefully dried with cotton, and the formaldehyde applied to the ulcer from a cotton swab well saturated but not dripping. This application is made daily until there is no sign of further extension; four or five applications are usually necessary. Care should be taken that the solution does not run back into the pharynx, and that the formalin gas is not inhaled; this may be prevented by plugging the throat or the nostrils with cotton wool.

The treatment appears to be highly efficacious even in advanced cases. In some instances sulphonamide drugs were also given but did not appear to have any curative effect, and in those cases in which they were not given the formaldehyde was just as effective as in the others. It was noticed that the smell of formaldehyde could be detected 24 hours after application and if the action of the gas liberated is important, it is considered that the retention of spongy necrotic tissue may be a help rather than a hindrance in that it tends to hold much more of the solution and to give off the gas for a much longer time than healthy tissue. *C. W.*

Velupillay (M.). **A Preliminary Note on the Treatment of Ulcers with Shark Liver Oil.**—*Jl. Malaya Branch Brit. Med. Assoc.* 1941. June. Vol. 5. No. 1. pp. 34–40.

Fifteen cases were treated; some of the ulcers had existed for years, others for a few months. All the patients were free from leprosy, syphilis and diabetes, and all had been treated by other methods, without success. Treatment consisted in mopping out the ulcer and smearing on shark liver oil, covering with oil-impregnated gauze or lint, cotton wool and bandages. These dressings were changed twice each week. If the ulcer was very foul it was cleaned with a mixture of pure Dettol, ½ ounce, and shark oil, 3 ounces. The Dettol is soluble in the oil and has effective deodorant properties, and this mixture can be used in place of the shark oil for a week or two until the ulcer is clean, after which shark oil alone is used.

Under this treatment granulation became active and there was rapid proliferation of epithelial tissue, even in callous and stationary ulcers. All except one of the ulcers were healed, the average period of treatment being 56 days. The author states that the vitamin A content of shark oil is from 4,000 to 22,000 I.U. per gm. compared with the 800 I.U. of cod liver oil, and it is to vitamin A that the healing of these ulcers is attributed. *C. W.*

Lages (Waldemar). Tratamento da ulcera tropical epidemica. [**The Treatment of Epidemic Tropical Ulcer.**]—*Brasil-Medico.* 1941. Aug. 23. Vol. 55. No. 34. pp. 582–583.

The author gives details of eight cases of tropical ulcer treated successfully by the application of sulphonamide preparations locally, combined with other sulphonamides taken by the mouth. He emphasizes that it is the combination of the two methods which is chiefly responsible for the favourable action. Sulphanilamide was the preparation chiefly used. *C. W.*

Riou (M.). Ulcère du cou de pied d'étiologie mixte chancrello-syphilitique. (Phagédénisme mixte tertiaire de Milian.) [**Ulcer of the Ankle of Mixed Aetiology.**]—*Rev. Méd. Française d'Extrême-Orient.* 1941. Mar.–Apr. Nos. 3–4. pp. 275–279. With 2 figs. on 1 plate.

The patient, a Corsican in Hanoi, contracted a mixed chancre of the penis. The bacillus of Ducrey was found, and his serum was positive for syphilis. One month after the onset, and before healing was complete, an ulcer formed over the left internal malleolus, which proved to be very resistant to treatment with arsenic, mercury, bismuth, Dmelcos vaccine, sulphonamides, X-ray and ultra violet light. In this ulcer bacilli morphologically identical with Ducrey's bacillus were constantly found, along with staphylococci, streptococci and Proteus. Anti-syphilitic treatment was pressed, and the ulcer finally healed after a course of sulphapyridine. The author considers that the staphylococci and streptococci were not merely acting as saprophytes; antisyphilitic treatment and Dmelcos alone were incapable of producing cure. *C. W.*

Mowat (A. H.) & Hennessey (R. S. F.). **Rhinosporidiosis in a Native of Uganda.**—*East African Med. Jl.* 1941. July. Vol. 18. No. 4. pp. 118–120.

This is believed to be the first case of Rhinosporidiosis in a native of East Africa, at any rate no previous record has been found. The patient was a Muganda peasant, 50 years of age, with obstruction of the left nostril due to a reddish, pedunculated tumour; the nasal sinuses showed thickened mucosa. At operation for its removal the growth was found to be attached to the floor of the inferior meatus at the front extremity of the inferior turbinate. Two months later a small recurrent nodule was appearing at the original site.

The tumour removed was rounded, 14 mm. × 8 mm. with a flat base, of a papillomatous appearance with fibromatous centre and covered by stratified squamous epithelium with branched processes, and in the interior cyst-like structures ranging from 12μ to 300μ, the larger having thick walls with large numbers of small nucleated bodies, 6μ or thereabouts in diameter, morphologically indistinguishable from *Rhinosporidium seeberi*. In the stroma of the tumour was infiltration with lymphocytes, macrophages and plasma cells, some polymorphonuclears and eosinophils. *H. H. S.*

Dhayagude (R. G.). **Unusual Rhinosporidial Infection in Man.**—*Indian Med. Gaz.* 1941. Sept. Vol. 76. No. 9. pp. 513–515. With 6 figs on 1 plate.

During the decade 1931–1940 the author has had 45 cases of rhinosporidiosis under his observation in Bombay. He records two as being of particular interest. The first was a Mohammedan male of 45 years with a pedunculated polypoid growth protruding from the urethra on micturition. It was found on examination to be about 2·5 cm. in length with a smaller one by its side, and situated 3 cm. within the external meatus. Histological examination revealed the typical features of a rhinosporidial papilloma. There was no growth in the nose or nasopharynx.

The second patient was a Hindu male of 40 years with swellings scattered all over the body ; he gave a six months' history, stating that the first swelling appeared on the left leg and they then became generally distributed, as small firm nodules, some of which broke down, suppurated and ulcerated ; their size varied from 1 cm. to 10×5 cm. There was no nasal or nasopharyngeal growth. Attempts at cultivation on various media, aerobically and anaerobically, were without success. The widespread character of the lesions disproved contact or lymphatic spread ; in fact, the only explanation seems to be extension by blood stream. The illustrations show the conditions clearly, and two photomicrographs depict the histological changes. *H. H. S.*

CARINI (A.). Sobre um parasito semelhante ao " Rhinosporidium," encontrado em quistos da pele de uma " Hyla ". [**A Rhinosporidium-like Parasite of a Hyla (Tree Frog).**]—*Arquivos do Inst. Biol.* São Paulo. 1940. Vol. 11. pp. 93–96. With 3 figs. on 2 plates.

The author found cystic enlargements in the skin of a tree-frog, closely resembling Rhinosporidium. He places it, he says, in the same group, but considering the distance in the zoological scale between the animal hosts of this (the Hyla) and rhinosporidium of man (*R. seeberi*) or horse (*R. equi*), he proposes to place it in a separate genus which he calls *Dermosporidium*, and this species *D. hylarum* [not a very valid reason for the creation of a new genus]. *H. H. S.*

DE SILVA (Stanley). **" Pseudo-Typhoid," a Ten Day Fever which is commonly mistaken for Typhoid Fever.**—*Jl. Ceylon Branch Brit. Med. Assoc.* 1941. Sept. Vol. 38. No. 3. pp. 319–323. With 1 chart. [Summary appears also in *Bulletin of Hygiene.*]

The author reports on ten cases of fever lasting for 10 days. The disease has the following characteristics : Young adults are the commonest victims, the fever (102°–103·5°F.) is of sudden onset without chill or rigor ; headache, frontal and severe, on the second to fifth days, face flushed, slight hebetude, tongue coated and dry, spleen palpable in some only, pulse " on the slow side " [rate not stated] no rash, temperature in evening 102°–103° for 4–5 days, then lysis to normal in 5 more, no complications or sequelae.

Laboratory findings were not helpful. Haemoculture in five gave no growth of any of the enteric group, agglutination of the same was negative [the author does not state at what stages during, or intervals after, the illness this was tried], Weil-Felix negative in two cases, no leucopenia but relative and absolute lymphocytosis (40 per cent. of 8,200) ; stool culture " proved negative in 4 cases " [presumably for members of the enterica group].

To label a febrile disease P.U.O., pyrexia of uncertain (not " unknown ") origin is, to say the least, unsatisfactory, for in most cases when the temperature falls and the patient recovers it is rare for further attempts to be made to solve the problem. To call it " pseudo-typhoid " is misleading for, as described, this disease has clinically few or none of the characters of typhoid fever—there are no prodromata, the onset is sudden, the duration is brief, the fever chart not at all like that of typhoid, toxaemia is slight, complications and sequelae absent, headache short-lived, abdominal symptoms lacking, no rash, no leucopenia.

[Clinically, the symptoms would suggest one of the dengue-sandfly fever group or a mild form of infectious jaundice (Weil's disease). More laboratory investigations are called for, such as attempts at culture of the virus on chorio-allantoic membrane for this may succeed 3–4 weeks after the onset of the fever, inoculation of the blood into monkeys and mice, and the mouse-protection test, agglutination of Leptospira, urine tests and so on; all these should be possible at a place like the General Hospital, Colombo.] *H. H. S.*

Sorol (Rafael V.). Epidemia de hepatitis en Tucumán. [**Outbreak of Hepatitis in Tucumán.**]—*Semana Méd.* 1941. July 17. Vol. 48. No. 29. pp. 151–154. [Summary appears also in *Bulletin of Hygiene.*]

In the latter half of 1939 and the first 4–5 months of 1940 there was an outbreak of hepatitis and jaundice in Tucumán. Notifications totalled 795, of which 550 were of men, 176 of women and 69 of children. The onset was febrile, with gastro-intestinal disturbance, nausea, vomiting, diarrhoea. All ages were attacked from less than one year to 65 years. In some the initial symptoms were influenzal in character with malaise and general lassitude; in others again the first noted sign was an unexpected jaundice with high-coloured urine. Some had constipation, others diarrhoea with pale, pasty stools. A few had bradycardia. The liver was enlarged, palpable one or two fingers'-breadths below the costal margin, and tender. The temperature was not high, 38°C. in the early days, and some had no fever. In those with fever the temperature fell by lysis. Treatment was on general lines, light diet, sulphate of magnesium for the constipated. There were no fatalities. The cause is at present unknown, but it is "infectious, hepatotropic and of benign evolution, distinct from catarrhal jaundice." *H. H. S.*

Rao (P. Krishna). **Infantile Cirrhosis of the Liver.**—Reprinted from *Proc. Indian Acad. Sci.* 1941. Vol. 14. No. 3. Sec. B. pp. 310–338. With 15 figs. on 6 plates. [52 refs.]

In view of the appalling mortality among children claimed by this disease, knowledge of its aetiology and pathology seems to be singularly defective.

The author has been investigating infantile cirrhosis since 1932 and has studied a series of 105 cases in the State of Mysore. It has now been confirmed that this condition is found to a greater extent among children in vegetarian families and to a less extent in non-vegetarians, but not in Moslems or Europeans.

It is peculiar to children between the ages of six and 24 months.

The onset is insidious and accompanied by constipation, but in the course of one to two months the liver is enlarged to the iliac crest and on palpation is smooth and hard. The spleen in some cases is also enlarged, extending to two fingers' breadth below the costal margin. About five months from the onset ascites, oedema of the face, hands, feet and eyelids become noticeable, and in the terminal stages after a course of eight to ten months, gastro-intestinal haemorrhages, cholaemia and icterus ensue.

The leucocyte count varies from 8,000 to 14,000 per cmm. in the early stages and may be as high as 50,000 in the terminal stages. The

increase is mainly due to lymphocytes (35–70 per cent.) with corresponding decrease in the polymorphs (25–50 per cent.) and the Arneth count shows a definite shift to the left. Among the red blood corpuscles microcytes predominate, but on the whole anaemia is not a feature.

At first negative, in jaundiced cases, the van den Bergh reaction becomes biphasic; the blood Wassermann is invariably negative, and on the whole the blood sugar is low. All routine tests and cultures of blood and faeces proved negative; but in the urine of four, *Bact. coli* was obtained and in one *Bact. alkaligenes*. The ascitic fluid was free from inflammatory cells. In one case where post-mortem examination was conducted half an hour after death *Bact. coli communis* was isolated from the liver substance.

Advanced case of cirrhosis of the liver with ascites and oedema of hands and feet, but no jaundice.

[Reproduced from the *Proceedings of the Indian Academy of Sciences.*]

Pathological studies were limited to four specimens of livers, owing to religious restrictions. [The section which represents good pathological research is illustrated by excellent photomicrographs.] Identical appearances were present in all specimens, which exhibited multilobular fibrosis with areas of necrosis and zones of regeneration (adenomata). The conclusion is that the clinical features combined with histological changes fulfil the criteria of portal, or Laennec's cirrhosis, so that it is suggested that the nomenclature should henceforth be "Infantile cirrhosis" instead of "Infantile *biliary* cirrhosis." In order to verify

whether the presence of bacteria in the liver might be due to post-mortem invasion, control cultures were made from 20 other cadavers, but in no single instance was *Bact. coli* obtained.

The author finds that the disease is met with in rich as well as poor—males and females being equally susceptible.

All were nourished on cows' milk from birth, but no single instance occurred in breast-fed infants.

Substitution of modern patent infant milk foods for cows' milk has prevented its occurrence in " infantile cirrhosis families."

Repeated pregnancies on the part of the mother do not form a predisposing fact, nor does bacillary dysentery play any rôle. The two important aetiological factors are cows' milk and invasion of the liver by *Bact. coli*.

[In a critical example quoted of twins—male and female—the latter fed on cows' milk, developed cirrhosis; the former, breast-fed, escaped.] *Philip Manson-Bahr.*

Ter Heege (F. H.). Tropische hooikoorts. [**Hay Fever in the Tropics.**] —*Geneesk. Tijdschr. v. Nederl.-Indië.* 1941. June 10. Vol. 81. No. 23. pp. 1231–1245. English summary.

" This article tries to give a short description of the history and of some causes of hay-fever in the tropical parts of the Kingdom of Holland, more especially Java.

" The symptomatology, the combination with multiple allergy and the therapy have also been described. Referred are 8 cases, in which cutis reactions were made with Zea mais, Sorghum andropogon, coffee (Robusta) and (or) tobacco pollens or their extracts. Two of these cases showed a seasonal rhinitis, coming back every year especially or principally during the dry period. In these cases only pollen reactions were made. The other patients showed a perennial rhinitis, for that reason they gave skin tests not only with pollens, but also with other inhalation and food allergens. In every case positive skin tests for one or more pollen were found. The patients suffering from perennial rhinitis, six cases, showed a multiple allergy.

" This means that hay-fever in the tropics is very often non-seasonal not only on account of the irregularity of the pollination periods but also on account of a multiple allergy directed against various antigens.

" The skin tests for other than pollen allergens are therefore more important in tropical than in non-tropical hay-fever.

" As for the treatment of hay-fever it may be supposed that seasonal as well as non-seasonal vaccination will have to be used, the method of one's choice depending on the individual history of the patient."

Williams (A. W.). **The Blood Pressure of Africans.**—*East African Med. Jl.* 1941. July. Vol. 18. No. 4. pp. 109–117. [11 refs.]

Essential hypertension is rare among African natives in Africa, but in the negroes of North America is as common as in the whites. Although there is a tendency to regard this difference as due to changes in mode of life and especially in diet, it may be that change of climate is more important, while altitude and physique are apparently correlated.

The author has taken blood pressure readings of 456 male and female natives of Uganda aged 16–50, and of 72 males over 50. All were

apparently healthy, and care was taken to obviate false readings, due to excitement, by taking several readings and counting only the last. The average systolic and diastolic pressures are given in tables for the different age groups, and the ranges of these readings are shown in the form of histograms which demonstrate wide differences about the averages. In general, it is evident that the average pressures are not significantly different, up to the age of 50, from those of the people of Europe or North America, and that in the older groups the steady rise in pressure which is found in Europe is not present in these natives. There is no evidence that diet is a factor, since natives on high animal protein diet show pressures similar to those on high carbohydrate. Similarly, altitude and skin colour seem to have no bearing, but external temperature and physique are apparently influential. *C. W.*

HARE (K. P.). **On the Importance of Malnutrition in the Aetiology of the Anaemic State in Tea Garden Coolies.**—*Indian Med. Gaz.* 1941. Sept. Vol. 76. No. 9. pp. 531–535. With 4 graphs. [Summary appears also in *Bulletin of Hygiene.*]

Anaemia is the rule in tea garden coolies and their families. Very young children are affected and it has been suggested that it may be congenital in origin. Of 111 children, most of whom were obviously undernourished, only 5·4 per cent. had a subnormal A.C.H. index, which once again suggests that this index is not reliable for use in India. The height for age and weight for age were lower than any recorded in India, but there was no close relationship between the height, weight, hip width and chest depth and the haemoglobin level. There was a slight but definite reduction (6·96 gm. per 100 cc.) in the Hb level of children showing signs of vitamin A deficiency as compared with those with no signs (7·20 gm. per 100 cc.). The average Hb. level was only three-fifths of that of Calcutta children of the same age. It tended to rise with age but the relationship was very irregular. There was possibly a relationship between the A.C.H. index and haemoglobin level in children with a similar hip width. The arm girth was the variable factor in the index (the chest depth was a fairly constant factor), which suggested some relationship between the animal protein intake and the haemoglobin level. The chief defects in the diet are in vitamins, protein and calcium and their relative importance in the production of anaemia may be in that order.

[The abstracter's conclusion is that these investigations give no clue as to the cause of the anaemia. It seems strange that the iron intake is not mentioned.] *H. N. Green.*

LACAZ (Carlos da Silva). Diagnóstico da molestia de Nicolas-Favre. Nota I: A reação de Frei. Nota II: Hemo-reações e histopatologia. Nota III: Exames sangue, liquor e fundo de olho. Nota IV: Inoculações experimentais. Propriedades do virus. [**The Diagnosis of Lymphogranuloma inguinale.**]—*Folia Clin. et Biol.* São Paulo. 1941. Vol. 13. Nos. 1, 2, 3 & 4. pp. 25–34; 48–58; 92–96; 119–124. [32 refs.] [Summary appears also in *Bulletin of Hygiene.*]

This article, or rather series of articles, consists mainly of a collating of records of the literature dealing with the Nicolas-Favre disease and

its diagnosis. The author treats the subject under the following heads: 1. The Frei reaction, the mode of preparation of the materials used, its application and interpretation. 2. Haemo- and sero-reactions—Ravaut, Reiss and Tulbermann. 3. The morbid histology of the lesions found in the disease, including the adenitis and the ano-rectal lesions. 4. Blood examination and the chemical changes in the spinal fluid. 5. Fundus changes. 6. Properties of the virus. 7. Experimental inoculation of laboratory animals.

The information given is already known to readers of this *Bulletin*, but it is useful to find it brought together in this way for reference.

H. H. S.

Briese (Reinhold R.) & Couch (James F.). **Mercuric Chloride as a Preservative of Cyanogenetic Plants for Chemical Analysis.**—*Jl. Agric. Res.* 1941. Apr. 15. Vol. 62. No. 8. pp. 493–507.

"A further study was made of the mercuric chloride method for preserving cyanogenetic plants for chemical analysis. Experiments were made with 14 varieties of sorghum, two species of wild cherry, and one species of arrowgrass. This study extends and confirms the results previously reported.

"On the whole, good preservation was obtained for periods up to 6 months and, in a number of cases, for 1, 1½ and 2 years. Young plants are more difficult to preserve than older plants. This is due to their higher content of hydrocyanic acid, to the rapidity with which it is developed in bruised tissues, and also to the fact that the cyanogenetic enzyme appears to be much more susceptible to the inhibiting action of mercuric chloride than is the case in older tissues.

"A concentration of 1 per cent. of mercuric chloride based on the weight of the plant sample is sufficient to preserve specimens that contain 100 to 125 mg. of hydrocyanic acid per 100 gm. Specimens that contain larger quantities of the acid require 2 to 3 per cent. of mercuric chloride for satisfactory preservation. Concentrations larger than 3 per cent. offer no advantages but have the disadvantage of markedly inhibiting cyanogenesis.

"The rate of cyanogenesis in the plants studied when they were preserved in 1 per cent. of mercuric chloride is such that in general the maximum amount of hydrocyanic acid is liberated in 3 to 8 weeks. With higher concentrations of the mercury compound the maximum quantity may not be attained for 6 to 12 months.

"The rate of cyanogenesis in the preserved samples could not be regularly increased by the addition of the appropriate enzyme to the sample.

"The cyanogenetic enzymes dhurrinase and prunase did not affect the stability of a solution of mercuric cyanide over a period of 15½ weeks.

"Mercuric oxide and mercurous chloride were less efficient as preservatives than mercuric chloride.

"The hydrogen-ion concentration of mixtures of sorghum and mercuric chloride falls within the optimum pH range for cyanogenesis in sorghum. The addition of mercuric chloride may be regarded as beneficial from this standpoint.

"Figures for the hydrocyanic acid obtained from samples of plants macerated in water, except for a few irregular cases, fall much below

those obtained by the use of mercuric chloride. Water maceration cannot be relied upon to furnish accurate data for the hydrocyanic acid content of cyanogenetic plants."

BROWNE (G. St. J. Orde). **Labour Conditions in West Africa.** Cmd. 6277. —149 pp. 1941. London: H.M.S.O. [2*s.* 6*d.*]

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